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POSTGRADUATE EDUCATIONAL NUMBER

British Journal of Anaesthesia

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Volume XXIX No. 12 December 1957

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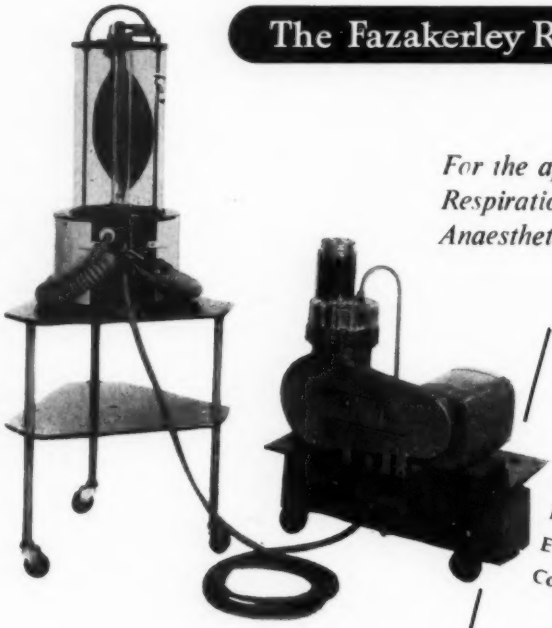

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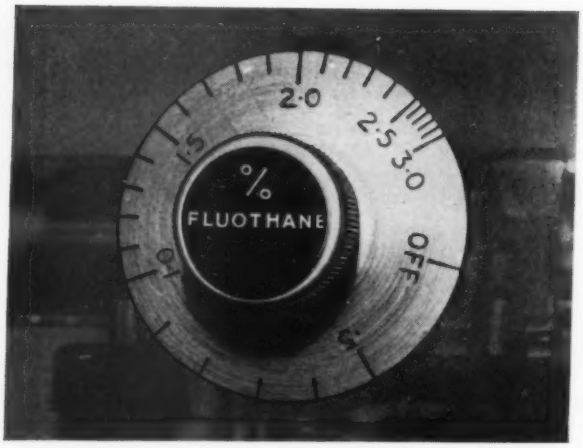

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BRITISH JOURNAL OF ANAESTHESIA

VOL. XXIX, No. 12 DECEMBER 1957

EDITORIAL

ANAESTHESIA thrives on several sciences, and the extent to which specialists have to delve into them increases materially as each subject enlarges. The assimilation of new knowledge and the assessment of its significance to anaesthetic practice also becomes more laborious because the range of concept and of vocabulary continually grows.

The time is fast approaching when it will become necessary for some sections of specialized communities regularly to pool and explain their knowledge in simple language, so that it can be made available for the general medical reader. Applied respiratory physiology is at present making rapid extensions and there is much in it of fundamental interest to the anaesthetist.

Comroe and his colleagues (1955) have succeeded in making applied respiratory physiology less difficult to comprehend. The reader who seeks to improve his knowledge of respiratory matters soon realizes his need for an appreciation of circulatory function, and this is not neglected in *The Lung*. Unfortunately there is at present no comparable monograph which deals with the circulation. However, those of our readers who became engrossed with the contents of the paper by Primrose (1954) will have their interest renewed by Brecher's (1956) recent monograph on *Venous Return*, which has been compiled from direct measurements made under conditions like those met with in anaesthetic practice.

The use of standardized symbols, first suggested by Pappenheimer and his group (1950), for applied respiratory physiology, have made it possible to express complicated equations in simplified form. Most authors now routinely use this nomenclature. Dr. Campbell, writing in this issue of the Journal, has exposed the need for care in extending the design of symbols to cover the mechanical problems of respiration.

A set of symbols to denote anaesthetic agents, techniques and inhalation circuits would prove invaluable to anaesthetists, because these would shorten the time taken to record data. This would be particularly useful during surgical operations when the rush to record, and at the same time to conduct the anaesthesia, causes much difficulty, usually to the detriment of the record. Most anaesthetists have developed a type of shorthand to enable them to do this, but the symbols vary. There is a need at the present time to design symbols for this purpose; it would be best to make it an international code, and it should not encroach on Pappenheimer's system.

Next year the Educational Numbers will be published in March and September. The March issue will contain a symposium on Emphysema.

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TERMINOLOGY AND SYMBOLS USED IN RESPIRATORY PHYSIOLOGY

BY

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INTRODUCTION

MANY anaesthetists have difficulty in following the recent advances of pulmonary physiology, not only because the subject is difficult, but because the physiologists use unfamiliar terms and mathematical expressions composed of strange symbols. Conversely, many papers appearing in anaesthetic journals which contain physiological studies, lose much of their value because terminology is not defined and insufficient information is given about techniques and the methods of expressing the results.

The aims of this article are: to stress the need for an agreed terminology and system of symbols; to explain those used by pulmonary physiologists; to give a glossary of terms and symbols of use to anaesthetists, and to discuss the difficulties met with in one branch of pulmonary physiology (the mechanics of breathing). It is hoped that this article will help anaesthetists in reading the current literature of pulmonary physiology and encourage them to observe the same conventions and use the same terminology.

WHY STANDARDIZE TERMINOLOGY AND SYMBOLS?

About ten years ago pulmonary physiology entered a phase of rapid progress. Quantitative studies and mathematical analyses of respiratory processes appeared in profusion, each with its own shorthand notation. Within a few years the experts could hardly understand each other, so in 1950 a group of American workers under the chairmanship of J. R. Pappenheimer put forward a suggested set of definitions and symbols. This system has now been in general use for seven years and, in spite of the continued rapid advance of the subject, it has proved not only adequate, but invaluable to workers in most branches of pulmonary physiology. The serious disadvantage of the system is that it does not adequately cover the mechanics of breathing.

There is a natural and understandable disinclination to change well-known words for new ones and to learn a new jargon of symbols. To practising anaesthetists, who do not usually need to think in exact or complicated mathematical ways, the advantages of a precise and standardized terminology are less obvious than they are to the physiologist. Nevertheless, little thought is necessary to appreciate that there are advantages in using terms based on a logical system which lends itself to the use of symbols. A consideration of terminology and the use of symbols in chemistry will make the point. It will be strengthened by an examination of table IV in which expressions in clinical use by pulmonary physiologists are shown. These equations would be unwieldly without the use of symbols. It is probably no exaggeration to say that much of the most penetrating work in the last decade would have been delayed if symbols had not been used to enable complex relationships to be examined in simplified forms.

SUBDIVISIONS OF THE LUNG VOLUME

The generally accepted definitions of lung volume are shown diagrammatically in figure 1. The primary subdivisions on the right are applicable to all conditions. There are no overlapping terms. The system on the left was introduced because there were a number of terms of established usefulness which included more than one primary subdivision. These were all standardized

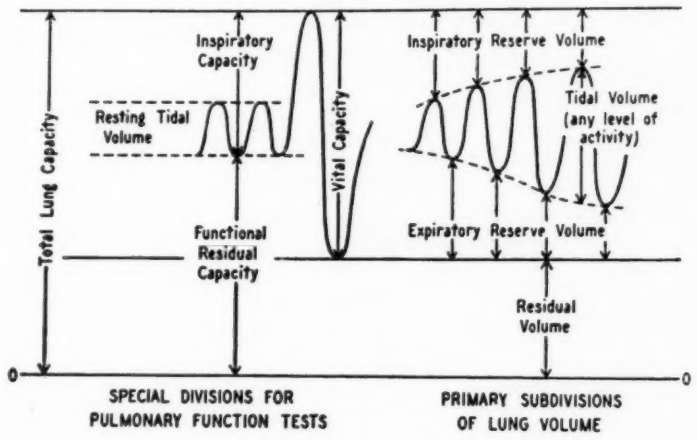

FIG. 1

as "capacity" terms. They should preferably only be used under fairly standard conditions—e.g. to describe the lung volume of subjects breathing normally in the sitting position. In table I the new terms are compared with others in use before 1950; the older terms were not logically related and some were ambiguous.

THE USES OF ATP, BTPS AND STPD

ATP (ambient temperature and barometric pressure) is the term used to describe the conditions under which a volume of gas is measured. ATPS applies to gases saturated with water vapour at the time of measurement; ATPD refers to dry gases. Volumes should preferably not be quoted at ATP, they should be corrected as described below. If they are quoted at ATP then the temperature and barometric pressure should be specified.

BTPS (body temperature and pressure, saturated with water vapour). These are the conditions under which volumes of gas exist in the lungs, and all results for lung volume determinations or ventilation volumes (e.g. tidal volume, dead space volume) should be quoted at BTPS. A table of correction factors converting ATPS to BTPS which can easily be converted into a graph, is given by Comroe et al. (1955). A rough correction for conditions usually found in operating theatres in Britain would be to add 9 per cent to the ATPS value.

STPD (standard temperature and barometric pressure, dry; i.e. 0°C and 760 mm Hg). These are the conditions which are used to describe quantities of individual gases exchanged in the lungs, e.g. the oxygen consumption or carbon dioxide output. This is the form in which the information is required for the analysis of physical and chemical processes. Correction tables giving factors converting ATP to STPD are to be found in several standard works on physiology and metabolism. They can easily be converted into a graphical form.

THE SYSTEM OF SYMBOLS NOW USED IN PULMONARY PHYSIOLOGY

Large capital letters are used to denote general respiratory variables such as pressure and volume. These are modified by attaching secondary symbols which denote location, molecular species or some special condition. The following conventions are employed for the secondary symbols.

(1) Localization in the gas phase is indicated by a small capital, e.g. pressure in alveolar gas is P_A.

(2) Localization in the blood phase is indicated by a lower case letter, e.g. pressure in arterial blood is P_a.

TABLE I
Lung Volumes (BTPS)

	Abbreviation	Standard term	Old term	Definition
1.	V_T	Tidal volume.	Tidal air.	Volume inspired or expired in a single breath.
2.	I.R.V.	Inspiratory reserve volume.	Complemental air. Complementary air.	Maximum volume that can be inspired from end-tidal inspiration.
3.	E.R.V.	Expiratory reserve volume.	Supplemental air. Reserve air.	Maximum volume that can be expired from resting expiratory level.
4.	R.V. or Rd.V.	Residual volume.	Residual air. Residual capacity.	Volume in lungs at end of maximum expiration.
5.	T.L.C. (1–4 above)	Total lung capacity.	Total lung volume.	Volume in lungs at end of maximum inspiration.
6.	V.C. (1–3 above)	Vital capacity.	Vital capacity.	Maximum volume that can be expired after maximum inspiration.
7.	I.C. (1 and 2 above)	Inspiratory capacity.	Complemental air. Complementary air.	Maximum volume that can be inspired from resting expiratory level.
8.	F.R.C. (3 and 4 above)	Functional residual capacity.	Functional residual air. Mid capacity. Normal capacity.	Volume in lungs at resting expiratory level.

TABLE II

I. *General variables.*
- V Gas volume in general, e.g. litres.
- $\dot{V}$ Gas volume per unit time, e.g. l./min.
- P Pressure in general.
- F Fractional concentration in the dry gas phase. (Easier to use than % because in calculations the division by 100 is obviated.)
- Q Volume of blood, e.g. litres.
- $\dot{Q}$ Volume of blood flow per unit time; e.g. l./min.
- C Concentration in blood phase.
- S Percentage saturation of Hb with O_2 or CO.
- f Respiratory frequency, e.g. breaths/min.
- R Respiratory exchange ratio (respiratory quotient).
- D Diffusing capacity.

II. *Secondary symbol for gas phase.*
- I Inspired.
- E Expired.
- A Alveolar.
- T Tidal.
- D Dead space.
- B Barometric.

III. *Secondary symbols for blood phase.*
- a Arterial.
- c Capillary.
- v Venous.

In each instance the exact site should be specified.

IV *Special symbols.*
- $\dot{X}$ Dot above means time derivative, e.g. $\dot{V}$, volume per unit time.
- $\bar{X}$ Dash above means a mean value, e.g. $\bar{v}$, mean (or mixed) venous.

A number of other special symbols are often used which are not standardized but should be specified in each publication.

(3) Molecular species is depicted by the full chemical symbol in small capitals, e.g. P_{CO_2}.

(4) If both location and molecular species are required then the symbol for location comes immediately after the main variable and that for molecular species appears last, as a subscript, e.g. $P_{A_{CO_2}}$ represents alveolar carbon dioxide pressure.

A list of those symbols in general use is given in table II. Table III is a list of derived symbols of use to anaesthetists. The only practical disadvantage of this system is that it is not adapted to the typewriter; however, this is easily overcome by the use of half spacing.

TABLE III

Useful terms for the Anaesthetist Abbreviated using Standardized Symbols.

Abbreviation	Definition	Usual units
V_T	Tidal volume.	ml or l. BTPS
V_D	Dead space volume.	ml or l. BTPS
$\dot{V}_E$	Expired volume per unit time (total ventilation).	l./min BTPS
$\dot{V}_A$	Alveolar ventilation per unit time.	l./min BTPS
f	Respiratory frequency.	Breaths/min
$F_{I_{O_2}}$	Fractional concentration of O_2 in inspired gas.	
$F_{I_{CO_2}}$	Fractional concentration of CO_2 in inspired gas.	
F_A	Fractional concentration in alveolar gas (eg. $F_{A_{O_2}}$).	
F_E	Fractional concentration in expired gas (eg. $F_{E_{O_2}}$).	
$P_{A_{O_2}}$	Alveolar O_2 tension (partial pressure).	mm Hg
Pa_{O_2}	Arterial O_2 tension (partial pressure).	mm Hg
Sa_{O_2}	Arterial O_2 saturation.	% capacity
Ca_{O_2}	Arterial O_2 content.	ml/100 ml
$\dot{V}_{O_2}$	O_2 uptake.	ml/min STPD
$\dot{V}_{CO_2}$	CO_2 output.	ml/min STPD
P_B	Barometric pressure.	mm Hg
Terms within the generally agreed system can easily be created, e.g.		
$F_{I_{N_2O}}$	Fractional concentration of N_2O in inspired gas.	
Pa_{N_2O}	Partial pressure of N_2O in arterial blood.	

TERMINOLOGY AND THE MECHANICS OF BREATHING

The system described above was introduced before the development of recent work on the mechanics of breathing. As a rule authors in this field define their terms and explain their symbols. Some tendency for terms and symbols to become accepted by usage is inevitable; this is helpful, but the symbols bear no necessary relation to others in pulmonary physiology. Little difficulty is presented to those acquainted with pulmonary physiology, but to others it would be confusing to read in one paper that

$$R = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}}$$

and in another

$$R = \frac{P_A - P_M}{\dot{V}}$$

In the first equation R refers to the respiratory exchange ratio; in the second it refers to the nonelastic resistance of the airways, which (in special circumstances) equals the difference in pressure between the alveoli and the mouth divided by the rate of airflow.

Furthermore, in the future development of the subject, ventilation—blood flow problems may be related to the mechanics of breathing. To have two sets of conflicting symbols may then be very unfortunate.

No useful suggestions can at present be given about symbols for use in relation to the mechanics of breathing. The problem is under discussion and, no doubt, an attempt will be made to reach an agreed system similar to that employed in the other fields of pulmonary physiology.

It is also difficult to give precise definitions of several of the terms employed in the mechanics of breathing because of the absence of any general agreement about the conditions of measurement. The following list of simple general statements should, however, assist readers unfamiliar with this field.

$$\text{Compliance} = \frac{\text{Change in volume}}{\text{Change in pressure difference}}$$

(At zero airflow)

The usual units are l. or ml/cm H_2O.

The structure whose compliance is derived from this calculation is governed by the sites between which the pressure difference is measured. For instance, if the lungs and chest wall are inflated from the resting position (at

TABLE IV

Some useful equations.

These equations are not intended to be read. They are included to assist workers in this field. Once the symbols are learned the equations follow easily. Other useful equations and more details of their derivation can be found in *The Lung* (Comroe et al., 1955).

I. Relation between fractional concentration (dry) and partial pressure of any gas x at **BTPS**

$$P_X = F_X\,(P_B - P_{A_{H_2O}})$$

(F is the fractional concentration of dry gas. When saturated with water vapour the total pressure of the dry gas is barometric pressure minus the water vapour pressure ($P_{A_{H_2O}}$). At 37°C the vapour pressure of water is 47 mm Hg.)

II. Relationships between total, alveolar, tidal and dead space ventilation

$$\dot{V}_E = f \cdot V_T$$

$$\dot{V}_A = \dot{V}_E - \dot{V}_D = f \cdot (V_T - V_D).$$

III. Relation between alveolar ventilation, alveolar CO_2 concentration and the metabolic production of CO_2 (*a*) and consumption of O_2 (*b*)

$$\dot{V}_A = \frac{\dot{V}_{CO_2}}{F_{A_{CO_2}}} \quad \ldots\ldots (a)$$

$$= R \cdot \frac{\dot{V}_{O_2}}{F_{A_{CO_2}}} \quad \ldots\ldots (b)$$

Apply BTP or STP corrections to (*a*) and (*b*). (Usually VBTP = VSTP × 1.2.)

IV. The Bohr equation for the calculation of dead space (for any gas X).

$$V_D = \frac{(F_{E_x} - F_{A_x})}{(F_{I_x} - F_{A_x})} \cdot V_T$$

Generally used forms of this as applied to CO_2

$$V_D = \frac{(F_{A_{CO_2}} - F_{E_{CO_2}})}{F_{A_{CO_2}}} \cdot V_T \quad \ldots\ldots (a)$$

or

$$V_D = \frac{(P_{A_{CO_2}} - P_{E_{CO_2}})}{P_{A_{CO_2}}} \cdot V_T \quad \ldots\ldots (b)$$

Equation (*b*) was derived from (*a*) by multiplying the fractional concentrations (F) throughout by ($P_B - 47$) to convert them to pressure or tension.

V. *Respiratory exchange ratio* (*respiration quotient*)

$$R = \frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}} = \frac{F_{E_{CO_2}} \cdot \dot{V}_E - F_{I_{CO_2}} \cdot \dot{V}_I}{F_{I_{O_2}} \cdot \dot{V}_I - F_{E_{O_2}} \cdot \dot{V}_E}$$

There are several other forms of this important equation. Most of them obviate $\dot{V}_I$ which is not usually measured. If the inspired mixture contains a neutral gas such as N_2 then in a steady state:

$$\dot{V}_I = \frac{\dot{V}_E \cdot F_{E_{N_2}}}{F_{I_{N_2}}}$$

VI. The Fick principle (as applied to calculation of cardiac output)

$$\dot{Q}a = \frac{\dot{V}_{O_2}}{Ca_{O_2} - C\bar{v}_{O_2}}$$

$\dot{Q}a$ in this case is the systemic arterial blood flow.

VII. The "alveolar" equation for calculating alveolar O_2 tension

$$P_{A_{O_2}} = P_{I_{O_2}} - \frac{P_{AC_{O_2}}}{R} + \left[\frac{P_{A_{CO_2}}}{R} \cdot F_{I_{O_2}}\,(i - R)\right]$$

This equation can only be applied when breathing a mixture of O_2 and a neutral gas, i.e. one which has a negligible net pulmonary exchange. The equation often appears in other forms. The advantage of this one is that the last term (in square brackets) is small and for approximate calculations can be neglected.

VIII. The diffusing capacity of the lungs for any gas X

$$D_X = \frac{\dot{V}_X}{P_{A_X} - \bar{P}c_X}$$

which alveolar pressure is P_A*) to a volume ΔV above the resting position, and the pressure in the alveoli ($P_{A'}$) is measured at zero airflow, then the compliance that will be measured is that of the combined or total lungs and thoracic cage.

$$\text{Total compliance} = \frac{\Delta V}{(P_{A'} - P_B) - (P_A - P_B)}$$

If oesophageal or pleural pressure (P_P) were measured, then the difference between intrapleural and alveolar pressure would give the compliance of the lungs.

$$\text{Lung compliance} = \frac{\Delta V}{(P_{A'} - P_{P'}) - (P_A - P_P)}$$

and the difference between pleural and ambient (barometric) pressure would give the compliance of the thoracic cage.

$$\text{Thoracic cage compliance} = \frac{\Delta V}{(P_{P'} - P_B) - (P_P - P_B)}$$

(Note the temptation to abbreviate compliance to C, which could lead to confusion with the the symbol for concentration in the blood phase).

$$\text{Elastic resistance (or elastance)} = \frac{\text{Change in pressure difference}}{\text{Change in volume (at zero airflow)}}$$

The usual units are cm H_2O per l.

Comparison of the definitions of compliance and elastic resistance will show that:

$$\text{Elastic resistance} = \frac{1}{\text{Compliance}}$$

Hence, the same conditions apply regarding the structure whose elastic resistance is measured as apply to compliance.

$$\text{Nonelastic resistance} = \frac{\text{P.D. at flow rate } \dot{V} - \text{P.D. at zero flow}}{\dot{V}}$$

(P.D. = pressure difference).

The usual units are cm H_2O/l./sec.

This equation is an approximation permissible only at low flow rates. At higher flow rates pressure and flow rate are related by more complex formulae.

The structure whose nonelastic resistance is derived by this calculation depends upon the sites at which the pressures are measured and upon certain other conditions. Thus the nonelastic resistance of the lung tissues and the nonelastic resistance of the airways can be estimated separately. An adequate definition of the terms employed would require an account of techniques used in the study of the mechanics of breathing which is outside the scope of this article.

SUMMARY

The desirability of using standardized terms and symbols in pulmonary physiology is outlined.

The standardized terminology used to describe the lung volumes is described.

The meaning and use of ATP, BTPS and STPD are described.

The symbols used in ventilation, blood flow and gaseous exchange studies are described.

Tables of symbols and equations which may be of value to anaesthetists are given.

The difficulties at present associated with the use of standardized terms and symbols in the mechanics of breathing are discussed. Some general definitions are outlined.

ACKNOWLEDGMENTS

I would like to thank Dr. J. F. Nunn and Dr. B. W. Peckett for reading the manuscript and making helpful suggestions. Figure 1 is reproduced by kind permission of Dr. J. R. Pappenheimer and the American Physiological Society.

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* P_A as used here refers to absolute alveolar pressure. Much work in the mechanics of breathing makes use of the convention that ambient pressure (barometric pressure, P_B) = O. Thus intrapleural pressure may be given as " -5 cm. H_2O ", which really means $P_B - 5$. (Some writers use the symbol ΔP to describe a pressure $P_B - P$.) In this section of the article absolute values are always implied by the symbol P.

Brit. J. Anaesth. (1957), **29**, 540

PHYSIOLOGICAL ASPECTS OF ARTIFICIAL VENTILATION

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UNTIL the end of the nineteenth century artificial ventilation was largely confined to resuscitation after asphyxial accidents. During the present century, thoracic surgery has stimulated the development of new methods and improvements of technique, and the last decade, in particular, has seen a remarkable increase in the practice of artificial ventilation. Respiratory arrest by drugs is now accepted as a routine procedure during anaesthesia and the anaesthetist has thus acquired great practical experience in the management of the apnoeic patient. His advice is usually sought in the management of medical conditions in which respiratory failure occurs or is a consequence of treatment.

The management of artificial ventilation is generally empirical. Measurement is the exception rather than the rule and minute volumes, carbon dioxide tensions and inflation pressures are usually judged by hand and eye in the light of clinical experience. In the majority of cases little difficulty is encountered. Every day in this country some hundreds of patients become apnoeic and return uneventfully to normal spontaneous respiration after a period of artificial ventilation. On occasion, however, the patient does not respond in this manner and most anaesthetists have seen patients who have remained apnoeic for prolonged periods. Sometimes it is not clear whether there is central or peripheral respiratory failure, carbon dioxide retention or depletion, or whether the apnoea is perhaps related to an abnormal Hering-Breuer reflex. In addition, little is known about the distribution of inspired gas and pulmonary blood flow during artificial ventilation, particularly when the chest is open and the patient is lying on his side. These problems are far from simple and Comroe et al. (1955), in discussing the raised arterial carbon dioxide tension of a patient undergoing thoracotomy, state that no conclusions can be attempted without complete data. Absence of data, to a large extent, limits the present stage of knowledge, although to the practising anaesthetist the questions to be answered are becoming clearer.

It is not possible to discuss all the methods of artificial ventilation and this article is confined to the passive inflation of the lungs by air pressure. Pask (1955) has described a wide variety of other methods which may come within the anaesthetist's province.

MECHANICAL CONSIDERATIONS

The lungs may be inflated by raising the pressure within the alveoli above the pressure of the atmosphere surrounding the trunk. Rhythmical inflation in this manner is usually referred to as ventilation by intermittent positive pressure (IPP). Alternatively it is possible to inflate the lungs by reduction of the pressure surrounding the trunk (below the pressure within the lungs) as in cabinet respirators. Each method depends upon the development of a differential pressure between the inside and outside of the chest and the two methods are therefore fundamentally similar.

As in spontaneous respiration, the work is done during inspiration. Expiration is normally passive and is motivated by the energy stored in the elastic tissue of the lung which has become stretched during inspiration. The work of inspiration is required to overcome two types of resistance which are most conveniently termed elastic and nonelastic.

Elastic resistance.

If a balloon is progressively inflated with air, the pressure inside is found to increase with each change in volume. The volume may be plotted against the pressure and over a certain range the relationship is linear (fig. 1). The

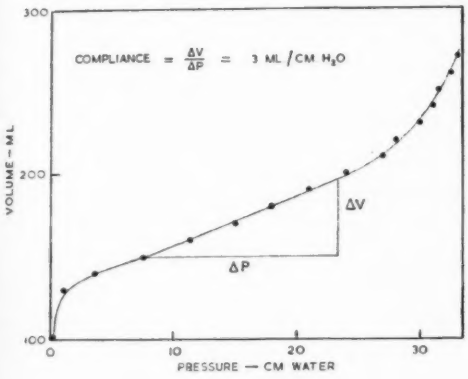

FIG. 1
The pressure-volume diagram of a toy balloon.

change in volume for unit change in pressure is termed the compliance and, in a pressure-volume diagram, is the gradient of the curve $\left(\frac{\Delta V}{\Delta P}\right)$. For the respiratory system the most convenient units are ml (or l.)/cm of water pressure. A low compliance indicates a " stiff " lung as in pulmonary fibrosis and a high compliance implies a loss of elasticity as in emphysema.

The excised lung behaves in many ways like a balloon and the intact lung will contract to a volume well below the residual volume when the pleura is opened and the intra-alveolar pressure equals the atmospheric pressure. In the intact subject the tendency of the lungs to contract is opposed by the elastic pull of the chest wall which expands them to a volume rather larger than the resting position. At the resting end-expiratory level the elastic pressures of the lungs and chest wall are equal and opposite, and the system is therefore in equilibrium with a subatmospheric intrapleural pressure. The lung volume in this position is called the functional residual capacity (FRC) which may be defined as the volume when there is neither muscular activity nor a difference in pressure between the alveoli and the atmosphere surrounding the trunk. Howell and Peckett (1957) found the FRC to be unchanged by muscular paralysis. It is, however, altered by posture and is increased in certain diseases associated with chronic difficulty in expiration, particularly emphysema and asthma.

The pressure-volume diagram for the intact subject includes lung volumes above and below the FRC with corresponding intra-alveolar pressures above and below atmospheric. Measurements of the intrathoracic pressure may also be made and the results are of interest in view of the effect of intrathoracic pressure upon the venous return. Several workers have studied the pressure-volume relationships of the anaesthetized and paralyzed human respiratory system (Nims et al., 1954; Butler and Smith, 1957; Howell and Peckett, 1957). The results are rather complicated and depend to some extent upon the manner of inflation, particularly its duration. Figure 2 summarizes the principal findings, but the reader is referred to the original articles as the results are not easy to present in simplified form.

Inflation to a volume near the normal end-inspiratory position will raise the intrathoracic pressure to atmospheric levels, and at larger tidal volumes there will be a further increase. At larger tidal volumes the pressure difference between the alveolus and the intrathoracic space (the transmural pressure) will increase and so

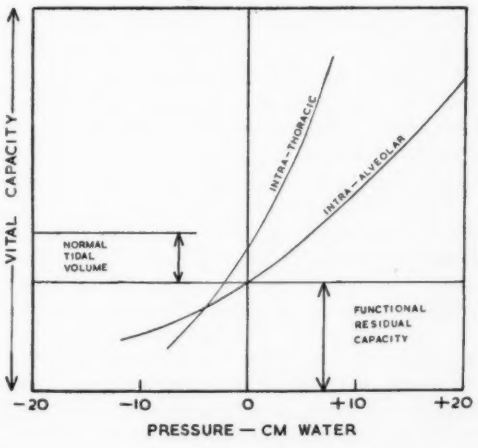

FIG. 2
Idealized pressure-volume diagram of the anaesthetized and paralyzed human respiratory system.

the intrathoracic pressure will not increase as much as the intra-alveolar pressure. On deflation to volumes below the FRC the behaviour of the system is complicated and difficult to understand (Butler and Smith, 1957). It is not possible to deflate the chest down to the normal residual volume, and at about half a litre below the FRC, the intrathoracic pressure rises above the intra-alveolar pressure, thereby reversing the usual transmural pressure gradient. Over the range of tidal volumes used clinically the compliance is almost constant and approximate calculations may be made to determine the *end-inflation* pressure required for a certain tidal volume. The end-inflation pressure is measured while no gas is actually flowing and takes no account of flow resistance which is considered later. The actual peak inflation pressure measured by the anaesthetist's aneroid manometer consists of the sum of the pressures required to overcome the elastic resistance and the nonelastic resistance. Only the former may be determined from the pressure-volume diagram.

The measurement of the compliance (of lungs and chest wall together) is comparatively simple when the subject is anaesthetized and paralyzed. The lungs are inflated to any suitable pressure which may be measured with a water or aneroid manometer. The patient is then allowed to expire into a spirometer and the tidal volume noted. The compliance is the tidal volume divided by end-inflation pressure. Butler and Smith (1957) describe the daily measurement of the compliance of a child with respiratory paralysis and were able to show a progressive fall in compliance (stiffening of the lungs).

The measurement of the compliance of the conscious subject is considerably more difficult, as any muscular activity will influence the pressure-volume relationship. With co-operative subjects it is possible to construct the so-called relaxation pressure diagram (Rahn et al., 1946). The compliance of the conscious subject has been found to be higher than that of the paralyzed subject (Nims et al., 1954; Howell and Peckett, 1957) (fig. 3). The cause of this stiffening in the paralyzed subject is not established but it is probably due to the abnormal pattern of inflation associated with artificial ventilation during paralysis of the respiratory muscles.

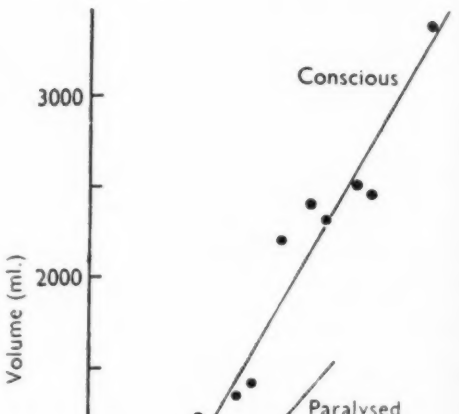

FIG. 3
The pressure-volume relations of the human respiratory system compared in the conscious and paralyzed states (Howell and Peckett, 1957; by kind permission from the *Journal of Physiology*.)

Nonelastic resistance.

The foregoing section deals only with the pressure-volume relationship under static conditions when no gas is actually flowing. The extra resistance during gas flow is most conveniently termed nonelastic resistance and comprises:

(*a*) Resistance to gas flow through the tracheobronchial tree.

(*b*) Resistance to movement of the tissues of the lungs and chest wall. (This factor is generally of little importance.)

Another negligible component is due to the energy required to accelerate and decelerate the movement of gases and tissues.

The nonelastic resistance to gas flow is measured as

$$\frac{\text{pressure difference required to maintain flow}}{\text{gas flow rate}}$$

and the usual unit of measurement is cm water/litre/second.

During laminar flow of gas, the resistance is constant at different flow rates, as the pressure difference required is directly proportional to flow rate (Poiseuille's Law). During turbulent flow, the resistance increases with flow rate, as the pressure difference required is proportional to the square of the flow rate. During normal respiration the flow is partly laminar and partly turbulent, and the resistance has been found to rise with increasing flow rates. The pressure required to overcome the resistance, therefore, increases more rapidly as the flow rate rises, and can be approximately represented by a quadratic expression.

Figure 4 shows typical curves of the pressure required to overcome flow resistance in normal and emphysematous subjects. The curves are compared with an example of purely laminar flow occurring in a smooth walled, relatively wide bore tube. In the latter the pressure bears a constant relation to the flow rate and the resistance is therefore the same at all flow rates.

Most methods of determining the flow resistance during respiration measure the sum of the resistances to gas flow and tissue movement. The total inflation pressure at any instant equals the sum of the pressure overcoming elasticity at the prevailing lung volume and the pressure overcoming flow resistance at the prevailing gas flow rate.

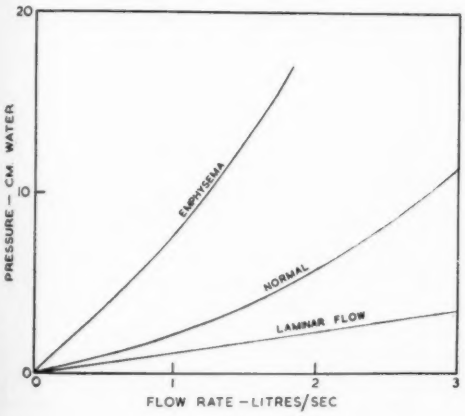

FIG. 4

Typical pressure-flow rate characteristics of the respiratory systems of normal and emphysematous subjects compared with purely laminar flow.

It has been shown previously how a simple manometer connected to the patient's airway may be used to measure compliance in the paralyzed patient. Information on the nonelastic resistance may be obtained by noting the maximum pressure required to inflate the patient.

If the tidal volume is approximately known, the elastic component of the pressure required for inflation may be determined from the pressure-volume diagram (fig. 2). If the peak inflation pressure occurs about half way through inspiration the elastic component of the peak pressure will approximate to half the total elastic pressure required for the chosen volume. The excess of the peak inflation pressure over this figure will thus indicate nonelastic resistance, and for practical purposes this may be assumed to consist largely of resistance to gas flow. The inspiratory flow rate will affect the pressure but with experience the manometer can be a reliable guide to flow resistance under operating theatre conditions. Although the method can hardly be regarded as quantitative, it has been found to be more sensitive than the anaesthetist's impression of resistance during manual inflation.

Resistance to gas flow may, on occasions, be greatly increased during anaesthesia or during the treatment of respiratory paralysis. Bronchospasm, accumulated secretion, or pus may be encountered and, in certain operations, the air passages may be inadvertently occluded from the outside. With inspiration the high pressure gradient from trachea to alveolus protects the inside of the thorax from the high inflation pressure and thus the venous return may not be impaired. However, if expiration is also impeded the lungs may not return to the FRC during the time allowed for expiration and this will inevitably result in a raised mean intrathoracic pressure.

The resistance to gas flow must include that due to apparatus. If such resistance is confined to inspiration relatively little harm can ensue, but if it is present during expiration, it may raise the resting expiratory level above the FRC in the same manner as resistance within the patient's respiratory tract.

Expiration.

During normal spontaneous respiration, expiration is passive and is carried out by energy stored in the stretched elastic tissue of the lung. The use of the expiratory muscles is confined to such acts as expiration to a lung volume less than the FRC; coughing and sneezing; speech; overcoming expiratory resistance in excess of 10–20 cm of water; breathing minute volumes in excess of about 50 litres/min (Campbell, 1957) and expulsive efforts.

Minor degrees of expiratory resistance do not require expiratory muscular work. The subject inhales more deeply and thereby stores more energy in the elastic tissues. Expiration does not proceed to the FRC but is cut short at a higher level which is raised in proportion to the resistance. Thus the whole tidal exchange occurs at a larger lung volume which may be predicted from the pressure volume curve of the paralyzed subject (Campbell et al., 1957). It is interesting to note that the extra work is done during inspiration.

Similar considerations apply to ventilation by IPP or by a cabinet respirator in which the pressure is not allowed to rise above one atmosphere. Purely passive expiration is sufficient for large minute volumes up to at least 20 litres/min, and moderate degrees of expiratory resistance may be overcome by inflation at larger lung volumes exactly as in spontaneous respiration. This method is widely employed during manual ventilation by anaesthetists, but suffers from the disadvantage of increasing the mean intrathoracic pressure, as the intra-alveolar pressure may not fall to atmospheric during expiration.

Expiration by the paralyzed patient against high resistance may require assistance by a subatmospheric airway pressure or by a raised pressure around the body in a cabinet respirator. Both have the effect of increasing the pressure gradient from alveolus to mouth and are analogous to the use of expiratory muscles by the conscious subject. If the resistance is mainly in the smaller air passages, as in emphysema, a sudden drop of pressure difference across their walls may result in their collapsing and so trapping gas in the alveoli. This is particularly likely to occur if the elastic tissue has been damaged by disease. A similar phenomenon occurs during a forced expiration in the conscious emphysematous subject when a spirogram, such as the example shown in figure 5, may be obtained. After a maximal inspiration a forced expiration may be arrested above the FRC by trapping. Had expiration proceeded in a more leisurely fashion, as in normal breathing, then the volume expired would have been greater. This is not to say that a moderate subatmospheric pressure during expiration is always harmful in emphysematous patients, but an abrupt fall of pressure may result in a decreased expiratory flow rate. Probably a " negative " pressure of 5 cm of water would be reasonable in emphysema or asthma, whereas the normal subject would not develop air trapping at a pressure 15 cm of water below one atmosphere. It is common practice to raise the pressure in cabinet respirators during expiration, and in terms of pressure differences between airway and the air surrounding the thorax, the effect must be similar to lowering the airway pressure.

If a subatmospheric airway pressure is maintained during expiration, the lung volume may be reduced below the normal FRC. It is theoretically possible for this to cause small areas of atelectasis, but in practice this does not appear to be a significant factor.

The electrical analogy.

To many who are accustomed to electrical circuits, an analogy helps to clarify thought about

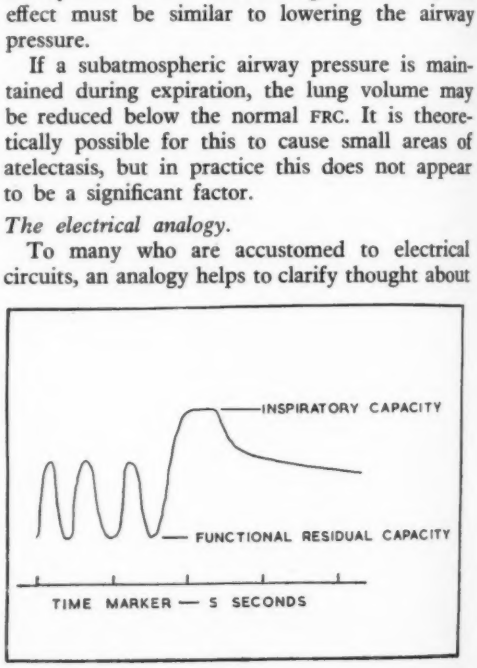

FIG. 5
The type of spirogram which may be obtained during a forced expiration by an emphysematous patient. Trapping occurs well above the functional residual capacity.

problems of gas flow, and in particular assists the development of quantitative relationships.

The circuit (fig. 6) consists of a potential difference which is applied to a condenser resistance network. This represents air pressure inflating the respiratory system. Volts represent pressure; ampères gas flow; ohms resistance; coulombs gas volumes; and farads (capacity of the condensers) are the equivalent of compliance. Zero potential (earth) represents atmospheric pressure.

The potential difference (V1) is applied through two resistances, R1 (endotracheal tube resistance) and R2 (tracheobronchial resistance) to two condensers in series (C1 and C2), which represent the compliance of the lung and chest wall. V2 represents the alveolar pressure and V3 the intrathoracic pressure. The charge built up in the condensers (in coulombs) is the equivalent of tidal volume and obeys time relations similar to those during inflation of the lung.

The nonelastic resistance to gas flow in the tracheobronchial tree (R2) is the pressure required to move the gas, divided by the flow rate. In the analogy the resistance (ohms) is given by the pressure drop (V4) divided by the current (A) which is flowing at the time (Ohm's Law).

The compliance of two structures in series (e.g. the lungs within the chest wall) is calculated from their separate compliances in a manner exactly analogous to capacities of condensers in series:

$$\frac{1}{\text{total compliance}} = \frac{1}{\text{compliance lung}} + \frac{1}{\text{compliance chest wall}}$$

For the sake of clarity the condensers have been shown without biasing cells which would be needed to maintain the equivalent of the subatmospheric intrathoracic pressure in the human subject.

CIRCULATORY EFFECTS

A raised mean intrathoracic pressure retards the venous return and consequently lowers the cardiac output (Beecher et al., 1943). Ventilation by IPP inevitably raises the mean intrathoracic pressure above the normal but the peripheral venous pressure rises and the venous return is thereby augmented. Maloney et al. (1953) found that, during IPP ventilation of fit male subjects, the cardiac output was not greatly reduced (mean fall of 12.4 per cent) and the blood pressure was well maintained. They then investigated three patients with circulatory inadequacy and found that IPP ventilation resulted in a serious fall in both cardiac output and blood pressure. They were able to demonstrate a remarkable recovery following the use of a subatmospheric pressure phase of about –10 cm water during expiration

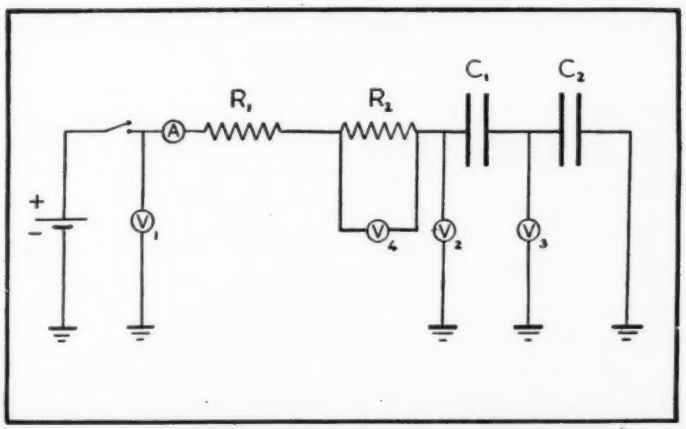

FIG. 6

An electrical analogy of artificial ventilation. For explanation see text.

which had the effect of reducing the mean intrathoracic pressure.

Apart from using a subatmospheric pressure during expiration the mean intrathoracic pressure may be kept at a minimum by suitable phasing of inflation. Sufficient time should be allowed for expiration to take place and generally this will require about double the time needed for inflation. The mean intrathoracic pressure will be unnecessarily high if the gas inflow time is prolonged. Inflation must therefore be short and with a rapid rise and fall. If pressure is plotted against time, this desirable state of affairs is represented as a square wave as opposed to a sine wave.

Apart from these measures the mean intrathoracic pressure can be lowered further only by a subatmospheric pressure during expiration. Just how important this is clinically is difficult to evaluate. The work of Maloney et al. (1953) is convincing but it is uncommon to encounter hypotension which is due to IPP. During a right thoracotomy in the lateral position it would appear impossible for the central venous pressure to be affected by inflation pressures. It is possible that in left thoracotomy the effect may be appreciable but this has not yet been investigated.

The venous return is affected, not by the absolute pressure in the right atrium, but by the pressure gradient from the peripheral veins to the right atrium. During IPP ventilation the pressure in the peripheral veins is not directly influenced by the inflation pressure and the venous return is thus opposed by the end-inspiratory pressure difference across the chest wall. In cabinet respirators the position is only apparently different. During the inspiratory phase the intrathoracic pressure falls to a value between atmospheric and the pressure in the cabinet. The peripheral veins, however, unprotected by the thoracic cage, are exposed to the full fall in pressure within the cabinet. Thus again the normal pressure gradient from peripheral veins to the right atrium is opposed by the pressure difference across the chest wall. Thus in each case, during inspiration, the venous return is opposed by a pressure which is probably the same for equal tidal volumes, and it would appear that the circulatory effects of the two systems of artificial ventilation should be identical. The magnitude of the effect may be forecast from the intrathoracic pressure-volume curve (fig. 2).

GAS EXCHANGE

The purpose of respiration is gaseous exchange and this is governed by three factors: ventilation, distribution and diffusion. Of these, ventilation is the only one under the direct control of the anaesthetist and consequently is of the greatest practical importance.

Ventilation.

The criterion of adequate gaseous exchange is the maintenance of normal oxygen and carbon dioxide tensions in the arterial blood. In the conscious subject respiration is very delicately controlled by the arterial carbon dioxide tension which is normally held between 36 and 44 mm Hg. The oxygen tension plays no part unless it is considerably reduced, a contingency which seldom arises under normal conditions. It appears to be reasonable to adopt the same criteria in the apnoeic as in the conscious subject, and to ventilate the patient so as to preserve a normal carbon dioxide tension. Should there be a serious fall in oxygen tension, however, this must take priority over any consideration of carbon dioxide homeostasis.

In many ways the elimination of carbon dioxide is a simpler process than the take-up of oxygen. It cannot be affected by poor diffusion nor is it seriously affected by minor degrees of maldistribution. As the carbon dioxide concentration in the inspired gas is, or should be, negligible, the alveolar carbon dioxide concentration must depend only upon the alveolar ventilation and the carbon dioxide output according to the equation:

$$\text{Alveolar } CO_2 \text{ concentration} = \frac{CO_2 \text{ output}}{\text{alveolar ventilation}}$$

Unless there is an error of inspired gas distribution the arterial and alveolar carbon dioxide tensions will be equal.

It is thus practicable to ventilate the patient with an eye to carbon dioxide homeostasis and if the oxygen tension falls (due perhaps to defects in diffusion or distribution), then steps may be taken to correct the hypoxia. This may be done

by alteration of the inspired oxygen concentration which is usually under the anaesthetist's control.

If the patient is hypoventilated the arterial carbon dioxide tension will inevitably rise and, conversely, hyperventilation will reduce the tension. Nunn (unpublished observations) has found that during anaesthesia, ventilation and end-tidal carbon dioxide tensions bear an approximately inverse relationship to each other, during both spontaneous respiration and artificial ventilation.

Campbell et al. (unpublished observations) found that anaesthetized patients ventilated by IPP maintained a normal arterial carbon dioxide tension with a minute volume lower than the pre-operative value. The reduction in the required minute volume was in proportion to the fall in carbon dioxide output. It would appear, on this evidence, that there is no reason for using a higher minute volume during artificial ventilation. It must, however, be stressed that the patients on IPP ventilation were intubated, were ventilated with negligible carbon dioxide in the inspired gas, and had less than 40 ml of apparatus dead space. These conditions do not always pertain during anaesthesia and with certain systems there is an appreciable concentration of carbon dioxide in the inspired gas (Bracken, 1956). Under such conditions relative hyperventilation may be required to maintain normal arterial carbon dioxide tensions. It is also probable that, during thoracotomy, the defects of gas distribution are so gross that it is wiser to hyperventilate as compensation for the uneven ventilation.

Dead space enters into the calculation of the required ventilation:

Alveolar ventilation
=resp. frequency (tidal volume−dead space)

The physiological dead space is more appropriately considered under "distribution" but the anatomical dead space may be dealt with here. It may be regarded as the part of the tidal volume which does not reach the alveoli, and for practical purposes must include the apparatus dead space measured up to that point in the inspiratory side of the circuit, which is free from carbon dioxide. It appears probable that the use of an endotracheal tube by-passes approximately half the anatomical dead space. The volume of endotracheal tubes, connections and valves may be determined by water displacement and the results will usually be found to be surprisingly high.

In conclusion, a normal subject with a closed chest should be ventilated at a minute volume close to the normal, and calculations for this have been made by Radford (1955). If the inhaled carbon dioxide concentration is appreciable, the anatomical dead space is enlarged or there is a gross error in distribution, then the patient must be hyperventilated. If there is hypoxia with adequate ventilation the inspired oxygen concentration should be increased.

Distribution.

During normal spontaneous respiration, there is remarkably uniform distribution of inspired gas and pulmonary blood flow. It is probable that under the conditions of artificial ventilation, deviations from this largely "ideal" state may occur, some alveoli being relatively overventilated and some relatively overperfused. The former constitute a dead-space-like effect and the latter a shunt or venous admixture effect. Although probably few alveoli are totally unperfused or totally unventilated, it is nevertheless, possible to express the distribution defect quantitatively in these terms. Relative overventilation is usually measured as extra dead space (in millilitres), and relative overperfusion as the percentage of the pulmonary blood flow which does not undergo gaseous exchange with the alveolar gas.

Recent observations by Campbell et al. suggest that a certain amount of maldistribution, particularly relative overventilation, occurs during IPP ventilation of fit subjects with intact thoracic cages in the supine position. It would seem highly probable that these effects would be more marked with an open chest, particularly in the lateral position. In the conscious subject in the lateral position both ventilation and perfusion are greater in the dependent lung; thus there is no gross impairment of ventilation-perfusion ratios. It is unlikely that this balance would be maintained with an open pleura and retraction of the lung, but few data collected under these circumstances are yet available.

The dead space effect. Hyperventilated alveoli are filled with inspired gas alongside and at the same time as normal alveoli. Much of the gas they contain is not available for gaseous exchange with the pulmonary arterial blood and thus they constitute what may best be termed the alveolar dead space. If the physiological dead space is determined from Bohr's formula (using the carbon dioxide tension of arterial blood instead of alveolar gas) the value obtained will equal the sum of the anatomical dead space and the alveolar dead space. Simultaneous measurement of the anatomical and physiological dead space is probably the most satisfactory method of determining the magnitude of relative hyperventilation.

With "ideal" ventilation and perfusion, arterial blood and alveolar gas have virtually the same carbon dioxide tension. If the expired alveolar gas is mixed with gas from relatively hyperventilated alveoli, the carbon dioxide tension of the mixed alveolar gas will be less than that of the arterial blood. This is referred to as an arterial-alveolar carbon dioxide tension gradient (or a–A P_{CO_2} gradient in accordance with the nomenclature of Pappenheimer et al. (1950)). It is of two-fold interest to the anaesthetist. In the first place it is a relatively simple method of detecting an alveolar dead space effect; and secondly, if it is appreciable, it must be considered when drawing conclusions about the arterial carbon dioxide tension from measurements made on alveolar gas. This is of practical importance, as clinical monitoring of arterial blood is not possible, whereas the continuous measurement of the alveolar carbon dioxide tension is feasible.

Few studies of the magnitude of the carbon dioxide tension gradient have yet been published but Severinghaus et al. (1957), in a study of five patients with atrial septal defects, report a mean gradient of 2.1 mm Hg in the conscious state and of 4.4 mm Hg after endotracheal ether during IPP ventilation, and 6.1. mm Hg during hypothermia with an open thorax and the lung retracted. Total overventilation of one lung occurs if the pulmonary artery of that side is obstructed during thoracotomy. This would cause a high a–A P_{CO_2} gradient. Provided that the remaining alveoli are adequately ventilated a dead space effect has comparatively little effect upon the arterial oxygen saturation.

The venous admixture effect. Relative overperfusion causes an admixture of venous blood with the mixed arterial blood. Normally this occurs to the extent of about 5 per cent of the cardiac output as a result of the bronchial circulation, the flow through Thebesian veins and some relative overperfusion which is always present. Pathological venous admixture occurs in congenital heart disease with a right to left shunt, pulmonary haemangiomata and relative overperfusion (or underventilation).

Simple calculations based on dissociation curves show that overperfusion has negligible effects upon the a–A P_{CO_2} gradient but considerable effects upon the oxygen tension gradient from the alveoli to the arterial blood (A–a P_{O_2} gradient) (Riley and Cournand, 1949). Absolute overperfusion of one lung, e.g. sudden occlusion of the bronchus with normal pulmonary blood flow would reduce the mixed arterial oxygen saturation to a point midway between that of the normal arterial and the mixed venous blood. Reference to the oxygen dissociation curve will show that this corresponds to a fall in oxygen tension of the order of 50 mm Hg.

Blood which is exposed to high oxygen tensions contains only slightly more oxygen than blood exposed to the normal alveolar tension of 100 mm Hg, as at that point the dissociation curve is almost horizontal. Thus, raising the oxygen tension in parts of the lung which are adequately ventilated will do little to compensate for parts of the lung which are totally without ventilation. Similar considerations apply to gross shunts such as occur with cyanotic congenital heart disease. Failure to improve cyanosis by giving 100 per cent oxygen may be regarded as proof that there is either a shunt or an area of lung without ventilation. If the overperfusion is not total but is relative over a considerable number of alveoli, then improvement will occur with a higher concentration of oxygen in the inspired gas mixture. This constitutes one of the indications for oxygen.

The presence of a venous admixture effect may be detected by demonstrating an abnormally high A–a P_{O_2} gradient. During thoracotomy there are ample opportunities for underventilation

by retraction of the lungs, kinking of the bronchi, and clamping of the bronchi before the pulmonary artery during pneumonectomy. Under these circumstances the pulmonary arterioles may be constricted and so deflect the pulmonary blood flow to other parts of the lungs which are adequately ventilated. It is doubtful whether this compensation is perfect, if it exists at all, and accidental intubation of the right bronchus is known to result in cyanosis which cannot be relieved by increasing the concentration of oxygen in the inspired gas mixture.

Diffusion.

The diffusing capacity of oxygen is the quantity of oxygen which passes per minute from the alveoli into the blood for each mm Hg pressure difference across the interface. It is a measure of the resistance to diffusion at the gas-blood interface and also of the number of alveoli available for exchange. Carbon dioxide, being more soluble than oxygen, diffuses about 21 times more readily and defective diffusion of this gas cannot be significant clinically.

To include diffusion in any comprehensive discussion of respiratory problems is customary, but during IPP ventilation it is unlikely that impaired diffusion could become an appreciable factor in the oxygenation of the patient. A capacity adequate to sustain life in a conscious patient would be more than sufficient for a paralyzed patient with a reduced oxygen consumption. The loss of diffusing area from massive collapse of several lobes of the lung would probably exert a negligible effect on the arterial oxygen tension compared with the effect due to the accompanying venous admixture. It is unlikely that the resistance at the alveolar capillary membrane would be increased significantly during a short time except perhaps by pulmonary oedema.

An increased oxygen concentration in the inspired gas mixture is the specific treatment for impaired diffusion. It has the effect of increasing the gas-blood pressure difference and directly counteracts the lowered diffusing capacity. Such treatment would not influence the elimination of carbon dioxide.

MONITORING OF VENTILATION

An understanding of the physiology of artificial ventilation is of limited value unless it is possible to measure certain quantities in clinical practice. The most significant measurement is the arterial carbon dioxide tension. This has the following advantages:

(1) The arterial carbon dioxide tension controls respiration in the normal conscious subject.

(2) The carbon dioxide tension is dependent almost exclusively on alveolar ventilation (assuming negligible inhaled carbon dioxide and a constant carbon dioxide production).

(3) The oxygen tension (which is dependent on the inhaled oxygen concentration, ventilation, distribution and diffusion) can be controlled independently of ventilation by adjusting the inhaled oxygen concentration, should this be necessary.

It has in the past been advocated that absence of cyanosis should be used as a guide to adequate ventilation. Not only will shunts and high inspired oxygen concentrations introduce large discrepancies, but even when ventilated with air the normal subject may have an arterial carbon dioxide concentration above 70 mm Hg before cyanosis is apparent. Furthermore cyanosis has been shown to be an unreliable indication of desaturation (Comroe and Botelho, 1947).

The arterial carbon dioxide tension.

The adoption of this measurement as a guide is unfortunately a counsel of perfection. Obtaining the sample should be neither painful nor harmful, but the subsequent methods of analysis all present difficulty.

(1) The direct method of Riley et al. (1945) depends on the analysis of a small gas bubble in equilibrium with the blood. Technically it is exacting and it cannot be applied in the presence of nitrous oxide. The usual error is ± 2 mm Hg.

(2) The indirect method is by substitution of values for the pH and the CO_2 content in the Henderson-Hasselbalch equation. In practice a nomogram may be used, and there are no mathematical difficulties. The determination of the CO_2 content is not critical and an error of 0.1mM/l. will affect the CO_2 tension (P_{CO_2}) by less than 0.2 mm Hg which is negligible. The measurement of the pH, on the other hand, is critical and an error of 0.01 pH units (which is low by most standards) will cause an error of the

order of 1 mm Hg P_{CO_2}. A method is available for the determination of CO_2 content in the presence of nitrous oxide (Orcutt and Waters, 1937).

(3) The P_{CO_2} may be determined from the pH alone if this measurement is made first on the original sample and then on the same sample after equilibration with a gas of known P_{CO_2}. The method is described by Astrup (1956) and requires pH determinations of the accuracy described above. This technique should be uninfluenced by the presence of anaesthetic gases and is more convenient than the indirect method.

The alveolar carbon dioxide tension.

The alveolar carbon dioxide tension can be measured with greater ease and more rapidly than the arterial blood tension. Results which take more than a few minutes to obtain are of limited value clinically. If there is a large alveolar dead space the arterial tension may be higher than the expired alveolar tension. The extent of this discrepancy under clinical conditions is as yet unknown. During the latter part of expiration with IPP ventilation the alveolar gas is of a reasonably constant composition and is often more constant than in the conscious subject. The carbon dioxide tension measured during this phase of expiration is known as the plateau value and, in the normal subject, it is very close to the tension of the arterial blood.

Plateau values may be determined by rapid continuous analysis or by sampling the latter part of expiration.

(1) Rapid continuous analysis will give inspiratory and expiratory CO_2 concentrations. The plateau value may be read from the tracing without difficulty. Infra-red analyzers (Collier et al., 1955) are the only rapid analyzers to be used for clinical monitoring at the present time.

(2) Various methods of end-tidal sampling are available which may be used clinically (Eastwood and Harbord, 1955; Inkster and Rees, 1956; Nunn and Pincock, 1957). With these methods it is possible to use simple analyzers without a rapid response time. The main drawback of end-tidal samplers is that they will not indicate patients who have emphysema. These patients do not have a constant expired alveolar carbon dioxide concentration and measurements on expired gas are of very little value.

Arterial blood pH.

If no method is available for the determination of carbon dioxide tension or concentration, it may be helpful to measure the pH of the arterial blood, provided that this can be done with an accuracy of ± 0.02 pH units. During hyperventilation the respiratory alkalosis is compensated by a metabolic acidosis, and in hypoventilation the respiratory acidosis is compensated by a metabolic alkalosis. The values obtained must be viewed in the light of this compensation which may develop within a few hours.

The CO_2 combining power or alkali reserve.

This measurement was introduced in the days when it was not possible to measure the P_{CO_2} directly or the pH accurately. It is the plasma CO_2 content (excluding dissolved CO_2) of oxygenated blood at a P_{CO_2} of 40 mm Hg, and is thus purely a measurement of metabolic acidosis or alkalosis. The CO_2 combining power measures not the imbalance of CO_2 due to hypo- or hyperventilation, but the metabolic compensation which occurs. Thus in ventilation problems a high CO_2 combining power shows a metabolic alkalosis which is probably the compensation for a respiratory acidosis due to hypoventilation. A low CO_2 combining power indicates a metabolic acidosis which may be the compensation for a respiratory alkalosis. Thus it will be seen that the concept of the CO_2 combining power carries with it considerable difficulties in the interpretation of the results.

The pH-bicarbonate diagram

The pH-bicarbonate diagram (fig. 7) which is lucidly explained by Davenport (1950) is very helpful in the understanding of the problems of acid-base balance. The abscissa is the pH and the ordinate the plasma bicarbonate (which is the CO_2 content less the dissolved CO_2 expressed as mm/l.). From the nomogram or the Henderson-Hasselbalch equation the isobars of CO_2 tension may be plotted, and from the CO_2 dissociation curve it is possible to draw the line followed by the normal subject as he under- or overventilates. This is called the normal buffer line. A patient in metabolic acidosis will move along a line parallel to and below the normal buffer line, while a patient in metabolic alkalosis will move along a line parallel to and above the normal buffer line. The alkali reserve of these patients would be the plasma bicarbonate at the point of intersection of the abnormal buffer lines with the isobar of P_{CO_2} 40 mm Hg; the normal value being approximately 24 m.equiv/l. Patients in metabolic imbalance commonly develop a respiratory imbalance to compensate and return the pH some way towards

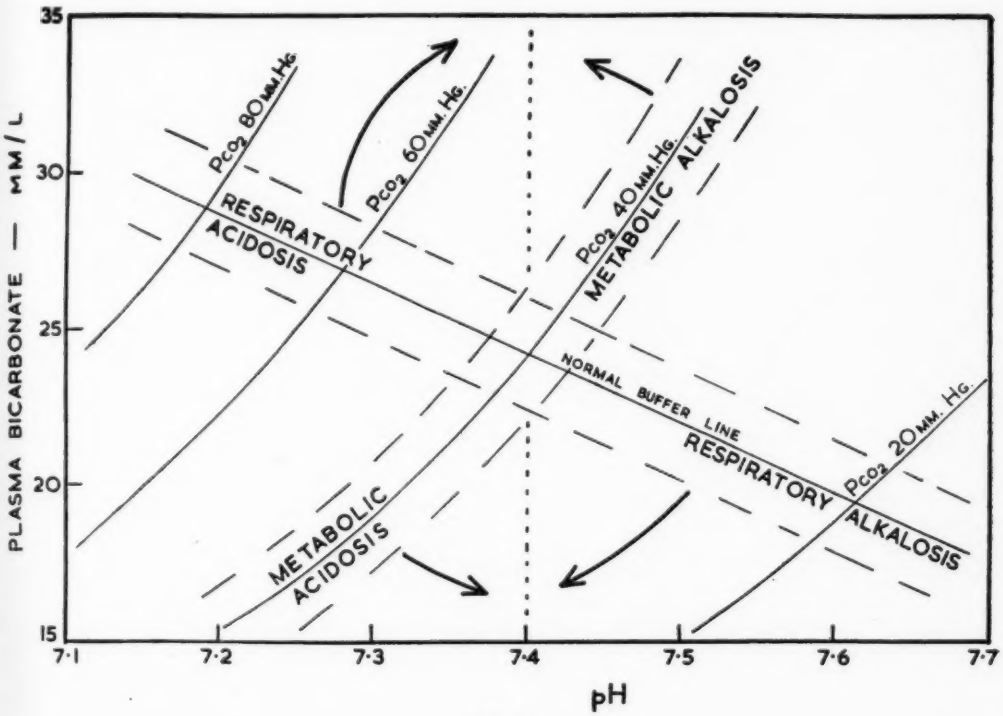

FIG. 7

The pH-bicarbonate diagram, showing both respiratory and metabolic acidosis and alkalosis. Compensations are indicated by the curved arrows. (Modified from Davenport, 1950)

the normal value. This compensation is shown by the two shorter arrows in the diagram. If values for the plasma bicarbonate and pH of a patient are persistently displaced along the normal buffer line into respiratory alkalosis or acidosis, the usual compensation is by a metabolic change which is indicated in the diagram by the two longer arrows. This restores the pH towards the normal value but remains along the same P_{CO_2} isobar as this is fixed by the ventilation and the patient's carbon dioxide output. It is this compensation which is measured as the CO_2 combining power and not the degree of respiratory acid-base imbalance (which caused the compensation in the first place). Measurement of any two of the three factors in the Henderson-Hasselbalch equation enables the values for the patient to be fixed on the pH-bicarbonate diagram and the third factor predicted. From this may be deduced both the respiratory imbalance and the metabolic compensation.

Minute volume.

Studies of arterial blood or alveolar gas usually require certain laboratory facilities and the result may not be available immediately. Ventilation, on the other hand, may be measured from minute to minute by the anaesthetist. It is true that this gives no direct information on the carbon dioxide balance of the patient, but clinically it is often an adequate guide, particularly with standards such as those of Radford which form a basis for computing the probable required minute volume.

With circle or nonrebreathing systems it is generally possible to incorporate a gas meter in either the inspiratory or the expiratory tubing (Zinberg and Jensen, 1954). Precautions must be taken to ensure that nothing but the tidal volume passes through the meter. In the case of anaesthetic circuits this often means some repositioning of the relief valve and of the inlet for fresh gases. Gas meters may be of the dry bellows or the rotary type like the Bennett respiration meter

or the anemometer of Wright (1955). A venturi meter has been described by Maloney et al. (1952); if no meter is available, a large spirometer may be used at the exhaust port of a non-rebreathing system.

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NEONATAL RESPIRATION AND HYALINE MEMBRANE

BY

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VOLTAIRE is reputed to have defined a bore as someone "incapable of leaving anything out". This subject has now become so large, however, that it would be impossible to avoid leaving gaps in any single account of it. Nevertheless we are still ignorant in much that remains to be worked out and can indulge in no more than tentative conclusions from such limited observations as we have been able to make.

There are many facets to be considered which provide a common interest for obstetricians, paediatricians, anaesthetists, physiologists and pathologists, all of whom are likely to be more or less directly concerned at one time or another. Hitherto there has been a danger that a divided interest should become a neglected interest, and until recent years a child's respiratory difficulties at birth have not received the attention which they deserve.

Respiratory disorders in the newborn have to be considered under two different headings. Firstly, there is failure to establish respiration satisfactorily. This is the category with which most of us are familiar because it is evident in the labour room at the time of delivery. Once respiration has been safely established, however, there is a greater tendency to assume that the child will either recover or die from causes outside our direct responsibility and control. The second category of respiratory disorder is failure to maintain respiration. The paediatricians have recently come to assume the lion's share of responsibility in this matter, but it would be a great mistake to divide respiratory difficulties into watertight compartments in the apportionment of responsibility. The paediatrician, for example, is often left literally holding the baby whose troubles are due to the accidents attending its birth, including anaesthetic accidents, for which the obstetrician and anaesthetist cannot disclaim responsibility.

FAILURE TO ESTABLISH RESPIRATION

Any baby which has even half a chance to breathe will almost certainly take it, often in spite of treatment and occasionally thanks to it. The changing fashions in resuscitative techniques testify to the newborn baby's respiratory stamina. Nevertheless it is necessary to recognize five prerequisite conditions for the satisfactory onset of respiration.

The first of these is a competent respiratory centre. This may be a difficult matter to assess and it is perhaps easier to consider the four factors in order of numerical importance which may render the centre incompetent. These are: antecedent anoxia; drugs and anaesthetics; raised intracranial pressure; and immaturity.

Antecedent anoxia. Often a baby is almost overcome by anoxia before the head emerges and gives it a chance to breathe, and many tragedies occur because no accurate method of assessing foetal anoxia before birth has yet been discovered. We still have to rely upon the observation of the foetal heart with its characteristic slowing and irregularity and the passage of meconium, but these are later signs, often too late, and their severity bears no direct relationship to the chances of imminent foetal death. Infants with these signs of so-called "foetal distress" can in some instances safely survive for hours, while in others the signs may be so transient as hardly to constitute a warning and yet a stillbirth may result. There is a great need for a more accurate assessment of the baby's state during the course of labour.

Certain conditions are well recognized for the way in which they interfere with the transfer of oxygen to the baby across the placental site. Hypertensive states and pre-eclamptic toxaemia inflict heavy penalties due to the reduced maternal placental blood flow as has been quantitatively demonstrated by radioactive isotope techniques

(Browne and Veall, 1950; Morris et al., 1955). Should an eclamptic seizure supervene, the effects of maternal asphyxia are superadded. These are causes which operate in late pregnancy so that the baby may start labour handicapped. In a similar fashion, though to a less certain extent, genuine postmaturity is believed to increase intra-uterine anoxia and Walker (1954) has demonstrated the reduced oxygen transfer to the baby in such cases. Postmaturity, however, as a foetal hazard cannot be reckoned as great as these investigations would suggest and the subject tends to be complicated by a number of other factors.

Placental separation whether due to placenta praevia or abruptio (commonly called "accidental") reduces the child's oxygen uptake in proportion to the amount of placenta separated, but where a placenta praevia happens to be posterior, compression by the presenting part is likely even more to reduce oxygen transfer. These causes often operate before labour starts and are almost wholly the obstetrician's concern. Sometimes, but not always they can be forestalled by early recognition.

During labour the baby faces the greatest risk of acute, as distinct from chronic, anoxia. Each time the uterus contracts it is believed that the transfer of oxygen to the baby is for the time being reduced. The resultant hypoxia tends to be cumulative in its effects, so that a colleague of mine once posed the question, "How many pains does it take to kill a baby?" There is clearly a limit to what even a robust baby can stand, especially after the membranes have been ruptured.

The hypertonic type of uterus is particularly vicious in this respect and its clinical recognition makes one take much more serious notice of the earliest signs of foetal distress because of the relatively bad accompanying foetal prognosis. Cord accidents are a fairly common cause of trouble and unfortunately cannot often be foreseen. Precipitate falls in maternal blood pressure, due to any cause, are obviously dangerous from the baby's point of view as well.

This list of causes of anoxic damage to the baby's respiratory centre would not be complete without emphasizing the disastrous effects of mismanaged anaesthesia.

Obstetric anaesthesia is far too often left in the hands of inexperienced people. A plentiful supply of unhappy reminiscences has convinced me that this can be one of the most treacherous branches of the anaesthetic art. The labouring woman usually has a full stomach. The more difficult her labour, the more likely she is to come to operative intervention in the end, and the greater will be the amount of fluid which the nursing staff will probably have coaxed into her by mouth. This fluid is poorly absorbed from the intestinal tract and, in copious brown quantities, lies in wait to be vomited back in the course of anaesthetic induction. This is a terrible hazard and a careful study of many maternal deaths, reading between the lines, leads one to the conclusion that inhaled vomit played a part in the disaster in spite of equivocal necropsy findings. Fortunately only a few die, but many more babies suffer from intense asphyxia during the desperate few minutes after such an accident in which the anaesthetist has to restore a satisfactory state of maternal aeration.

It is this hazard from inexpertly given anaesthesia which so commonly dogs our maternity units and has led to the increasing use of pudendal block anaesthesia in forceps delivery, a technique to which we in Glasgow have become very attached in the last few months. The characteristic respiratory liveliness of the baby is certainly an incidental reward. I feel, however, that this opportunity should not be lost of reiterating the need for more generous and expert anaesthetic cover for maternity units throughout the country. This is no job for the occasional anaesthetist.

Effects of drugs and anaesthetics. Apart from regional anaesthetic techniques, which have their own peculiar penalties, there is no such thing as the drug or anaesthetic agent which is both effective in relieving maternal pain and completely without effect upon the baby's respiratory activity at birth. It seems we can never get anything without paying for it and the choice and timing of the method of analgesia calls for more judgment than is commonly exhibited. These effects upon the normal, mature and healthy baby are slight and transient so that no serious hazard has to be considered but we are, nevertheless, certain

from our own observations that even a drug as reputedly harmless as trichloroethylene can not only seriously slow down labour but may produce a relatively unresponsive baby. With the brake now released on the use of trichloroethylene we may presently come to recognize this effect more fully.

When the baby is already in some jeopardy, either from antecedent anoxia and prolonged foetal distress, or from the trauma of a difficult birth, drug depression may not only make resuscitation difficult, prolonged, varied in method and therefore dangerous in itself, but may tip the scales against survival. This applies with even greater force in the case of premature delivery.

True, we have to our aid now the dramatic help of nalorphine to abolish the effects of pethidine and drugs of the morphine class, but it is a sobering reflection that the safest way of entering this world is in the sort of labour that can afford to do without obstetrician and anaesthetist.

Intracranial pressure. Any extensive rise in intracranial pressure obviously depresses the respiratory centre. The most flagrant cause is haemorrhage from tentorial tears and this, perhaps fortunately, is presently fatal although lesser degrees may leave a surviving child with serious neurological handicaps. Prolonged asphyxia, however, of itself produces widespread areas of petechiae and haemorrhage to the detriment of the central nervous system, and is accompanied by increase in intracranial pressure. Cerebral oedema, present in prematurity, maternal diabetes and in traumatic delivery, also adds its quota of mischief and makes the commonly used head down position in resuscitation of somewhat doubtful value.

Immaturity. The premature baby's respiratory centre has additional shortcomings. Its functional development is not complete until the last few weeks of pregnancy. It is now believed there are four developmental levels (Barcroft, 1946) extending upwards from the most primitive spasmodic and gasping centres, up through the centre of rhythmical control of breathing to the latest formed inhibitory centre, which discourages deep intra-uterine respiration until its inhibiting influence is overpowered by the stimuli which accompany or, preferably, follow birth. It follows, therefore, that the premature baby is not only likely to indulge in harmful deep inspiration of liquor amnii under the stimulus of labour, but that the operative functional level may be no higher than the gasping centre. The more mature and higher centres can also be put out of action by anoxia, drugs and trauma—an ugly sequence which is also demonstrated in the mature child born in severe asphyxia and foetal shock—but the process is more deadly in the premature infant.

Patent airway.

So much for the respiratory centre. The second of the five prerequisites for the establishment of respiration is a patent airway. It would be superfluous to preach to anaesthetists about the importance of this. Of all the varied measures now available in the resuscitation of the newborn none can match airway clearance in importance. Unfortunately this is often so very inefficiently carried out in many maternity units. During this process the head down position of the child is valuable in order to discourage aspiration of foreign material before it can be sucked out.

The traditional mucus catheter, as used by midwives, is a dirty and inefficient affair and the amounts of material removed by this instrument seem to be a poor quantitative return for all the noisy blowing and sucking that accompanies its use. The end of this catheter is quickly occluded by sticky foreign matter and has to be cleared by the midwife blowing down it with her own bacteriologically questionable mouth, thereby interfering with the aseptic technique of the labour room. The suction generated is seldom high enough to be efficient and is often applied blindly and in the wrong places. The one obvious benefit from this ritual is the shock of outraged surprise which it inflicts upon an otherwise docile and perhaps too sleepy infant so that it coughs and splutters. I suspect that tickling its throat and nostrils with a feather (sterile!) would be almost as effective. These remarks are not meant to decry the value of suction aspiration which can be life saving, especially if done under direct vision with the help of a laryngoscope, but the suction, to be adequate, is best supplied

by a mechanical device, such as a venturi attached to a gas cylinder which is instantly available, or by piped suction from a wall fitting. These methods ought to be available in all maternity units. Suction pressures as great as minus 90 mm of mercury are safe provided that they are applied through a small soft rubber catheter (e.g. No. 4 French) whose end is cut off square and not bevelled. A square-ended catheter tip is very much less likely to block itself by drawing in a fold of mucous membrane.

The suction catheter should not only be used to clear the pharynx of blood, mucus and meconium, but should be inserted thereafter into each nostril where, as an incidental benefit, the snout reflex noted in sheep by Barcroft (1946) may be evoked. Following this it is our practice, especially following delivery by Caesarean section, to pass the suction catheter down the oesophagus into the stomach in order to empty it. The danger of regurgitation of stomach contents and aspiration down the trachea by the baby is considerable when, for any reason, the cough reflex is in abeyance or depressed. It was shown by Gellis et al. (1949) that babies born by Caesarean section had relatively full stomachs, the babies so born of diabetic mothers doubly so, and that even vaginal delivery by forceps operation was associated, though to a lesser extent, with a volume of gastric contents greater than in spontaneous vaginal delivery. Although we have not confirmed the large quantities (up to 14 ml) reported by these workers, we nevertheless agree that the amounts which can be thus aspirated from the stomach are often much increased in these circumstances.

Mechanical suction is an institutional necessity and certainly more than a luxury, but it is, of course, not available in domiciliary practice. This is less of an argument against efficient suction aspiration than against domiciliary midwifery.

Peripheral circulation.

No amount of oxygen, howsoever given, will avail much if it cannot reach the vital centres of the brain for want of an adequate peripheral circulation. Unfortunately the worst clinical feature of the so-called "asphyxia pallida neonatorum", better termed "foetal shock", is just this very thing, namely, peripheral circulatory failure. If this had been better understood in the past many of the less rational resuscitative techniques would have been abandoned long ago. The pallid, grey appearance of the baby, its utter limpness and occasional gasping, often with a sideways jerk of the head, make up the desperate clinical picture of foetal shock. The heart beat is now very slow and any improvement in the baby's condition is accompanied by acceleration of the heart rate, which gives a far better and more immediate indication of the clinical condition than the colour of the skin, lips and nail beds. In other words, as one watches the peripheral circulation improve one notes incidentally, and later, the improvement in colour and with it the return of muscle tone.

Any safe and effective treatment which could restore an efficient peripheral circulation would go far towards pulling a child out of its crisis but we have little to fall back on therapeutically. Nikethamide and other such analeptic drugs are undoubtedly efficient but they are also convulsant and may not be altogether safe. Much will depend upon the underlying causes of foetal shock and the possibility of intracranial bleeding which is unlikely to be benefited by such treatment. Reports are awaited of treatment with noradrenaline.

Eve's rocking method (Eve and Forsyth, 1948) is reckoned to improve the circulation mechanically and has been applied in the case of the newborn (Roberts, 1949), but it has not been found possible to measure the benefit quantitatively—a criticism which applies to other methods of resuscitation.

In the majority of cases, therefore, it will be seen that peripheral circulatory failure is treated by watchful and none too hopeful expectancy, the stricken child being handled with the warmth and care which its "shocked" condition demands and being left to fight out its own salvation.

Respiratory movements.

The fourth prerequisite for the establishment of respiration is that respiratory movements should be adequate. To some extent this condition depends upon a competent respiratory centre, since poor efforts at breathing may be due to central causes. Other factors, however,

may interfere with efficient respiratory movement such as a large diaphragmatic hernia, for obvious mechanical reasons (fig. 1), but chief among all is the softness of the thoracic cage in cases of marked prematurity, often combined with muscular weakness.

The premature infant's ribs and sternum may be so soft that the spirit and muscles may be willing but the bony cage too weak to provide the necessary mechanical purchase for pulmonary expansion.

Atmosphere breathed.

The fifth and last prerequisite, by far the least important of the five, is the quality of the atmosphere to be breathed. Honest to goodness air is adequate for most babies and would suffice for all, provided that the other four conditions were met. It is where respiratory activity is insufficient to maintain life that enrichment with oxygen is called for.

Nobody now considers that admixture of carbon dioxide serves any purpose as a respiratory stimulant at birth. The asphyxiated child is already poisoned almost to death with it. Pure oxygen can be used in the immediate emergency but should be discontinued as soon as the "bitterness of death is passed". Maintenance therapy with oxygen is thereafter continued with concentrations not exceeding 40 per cent oxygen because of its irritant effect and the dangers of producing blindness from retrolental fibroplasia in the premature.

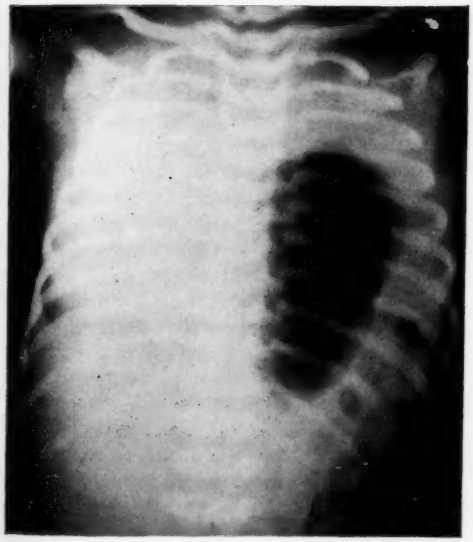

FIG. 1
Diaphragmatic hernia.

THE FIRST BREATHS OF LIFE

So far, more attention has been paid to the pathology of birth asphyxia than to the physiology of the start of respiration. This may be putting the cart before the horse, but is understandable because of the all too plentiful supply of necropsy material for study. The technical difficulties of attempting to make scientific observations, as distinct from clinical impressions, upon the first take-over by the baby of its own oxygenation are obviously considerable. We have studied this process by radiography, spirometry and electromanometry of pressure changes within the thorax.

As a result of our studies we believe, as do the pathologists Potter (1952) and Claireaux (1954), that in the fit mature baby pulmonary expansion is rapid at birth and takes place within a matter of minutes. In the case of the premature baby expansion is less rapid, but even so, provided that such a baby is vigorous in spite of its prematurity, a very fair degree of pulmonary expansion is radiologically demonstrable within the first two hours of life.

The radiographic study of neonatal lungs requires an efficient mobile X-ray unit since, under the exigencies of the investigation, the machine must be brought to the baby rather than vice versa. The ordinary standard apparatus is not suitable because of too long an exposure time on what is, after all, a very unstable target. We have been fortunate in acquiring a rotating anode machine, thanks to the generosity of the Board of Management of the Royal Maternity and Women's Hospital, Glasgow, where this research is now being carried out. Figure 2 is such a radiograph of a mature baby taken one minute and fifty-five seconds after birth, which is about as early an X-ray as one can get, allowing for positioning of the child. Already it will be seen that pulmonary expansion is well advanced although not yet complete, nor has there yet

been time for the stomach and intestinal tract to fill with gas, due to the swallowing of air. Within a few minutes, and depending upon the vigour of the child's crying and respiratory activity, the stomach and intestines will fill with air. In any case in which this phenomenon is not observed on X-ray, the lungs being at the same time well expanded, a suspicion of some congenital anomaly, such as oesophageal atresia or tracheo-oesophageal fistula, should be entertained.

Totally unexpanded lung is uniformly opaque and the cardiac shadow cannot easily be made out against the solid background. Primary atelectasis, if not too severe, has a ground glass appearance. Fuller degrees of aeration thereafter tend to become more patchily distributed as figure 2 shows. More use might well be made of radiography in studying normal pulmonary expansion after birth were it not for the radiation hazards involved. Since the work of Stewart et al. (1956) we have felt less inclined to pursue this matter as far as we might otherwise have liked.

Mediastinal pressure changes. The study of these has exercised us greatly since we believe that respiratory effort can be quantitatively assessed by measuring the pressure swings within the thorax through whose medium pulmonary ventilation occurs. It would be indefensible to introduce a cannula into the pleural cavity and we have made our measurements transoesophageally, having modified the method described by Dornhorst and Leathart (1952) who first used it in their study of emphysematous adults. The technique consists in passing, via the mouth or nose, an open-ended portex catheter of 1 mm bore which is connected to an electromanometer. The catheter should be passed about half way down the oesophagus. Dornhorst and Leathart kept their catheters full of a column of water, but we found this unmanageable in any but the quietest babies, since mechanical movement of the catheter produced artefacts in our tracings due to the weight of the water within the catheter and its viscosity.

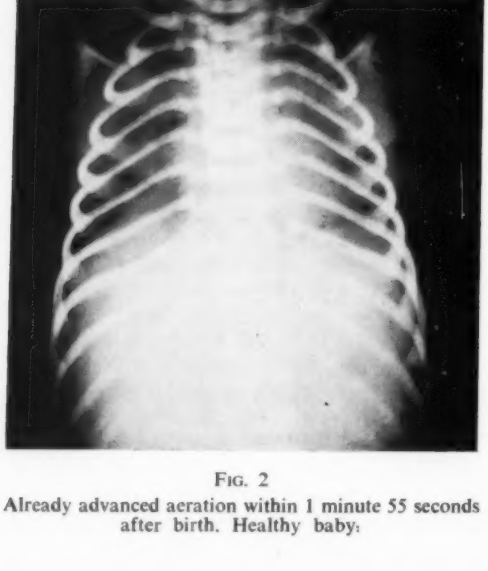

FIG. 2
Already advanced aeration within 1 minute 55 seconds after birth. Healthy baby.

We have now had about eight months' experience of our present method, which is to connect the upper end of an air filled catheter to a three-way tap. While passing the catheter, which we have many times achieved through a nostril as soon as the head is born and before even the shoulders appear, we keep the tap in the shut-off position. This discourages the flow of mucus up the catheter. When the catheter is satisfactorily in position the three-way tap connects up a 10 ml syringe by means of which 3 ml of air are smartly injected down the catheter. This usually succeeds in blowing out the bead of mucus which has been scooped into the lumen of the catheter during its passage and allows a small air bubble to be formed within the oesophagus around the open ended tip, thus providing a temporary but highly satisfactory tambour. The three-way tap is now turned to connect up the electromanometer and readings are taken. The 3 ml air bubble is soon passed on naturally into the baby's stomach and presently recordings will cease because of mucus entering the end of the catheter. This is remedied by injecting a further 3 ml of air to clear it and to reform another bubble tambour.

Sometimes it is possible to get readings lasting several minutes before more air has to be injected.

The great advantage of this technique is that, the transmitting medium being air and therefore "weightless", movements by the baby and changes in level relative to the manometer do not cause recorder deflections nor shifts in base line.

This great advantage more than compensates for a lowered frequency response, which would not matter in any case in respiratory investigations, and under-registering due to gas compressibility. The pressure changes being measurable only in centimetres of water, the error (which is always on the minus side) is not large and our measurements conform well to those which we obtained, with difficulty, by the old water transmission technique.

The choice and development of electromanometers and their amplification systems have cost a great deal of time, money and effort. Painfully, we have worked through and discarded most of the standard electronic systems for one reason or another. We began with unbonded strain gauges but suffered a great deal of trouble with amplifier instability, transferred to a photo-electric system with a mechanically chopped light source, tried transducer valves but were seriously bothered with drift, and later began to do quite well with a differential transformer type manometer (R. T. Electronics). This last has served us well and continues in use. Nevertheless for a variety of other purposes, and for reasons of economy, we have been at pains to produce a manometer of our own design. This has been achieved by Dr. Greer, physicist in our department, and consists of a very simple, cheap and highly ingenious optical and photo-electric system. It is being prepared for independent publication.

Briefly, the Greer manometer consists of a terylene diaphragm, silvered on both sides. The diaphragm is distorted first to one side on, for example, negative inspiratory pressure, making one surface slightly concave and the other surface convex, and then, as the pressure changes on expiration swing over to the positive side of zero, the diaphragm distorts in the opposite direction making the silvered surfaces respectively convex and concave.

Parallel light beams emanating from a common light source are arranged by means of mirrors and lenses to fall simultaneously on to both sides of the diaphragm whose infinitesimal distortions under pressure reflect the light as a convergent beam from the side which is now concave and at the same time as a divergent beam from the side which is convex. Each of these beams is arranged to fall on balanced germanium photo cells. The convergent beam will supply a more intense light than the divergent beam and the differences will unbalance the output from the two cells, thus giving a signal output which is proportional to the original diaphragm distortion and corresponding to positive and negative pressure swings about the central zero or neutral position.

This kind of manometer with its amplifying system is operated from mains electricity and since the light source is common to both sides of the silvered diaphragm and to both balanced germanium cells there is no instability nor drift due to mains voltage irregularities. There are no fragile nor expensive and irreplaceable parts and the whole machine is robust and compact. It is ideal for measuring small gas pressures on either side of zero centre, and therefore for respiratory research. It recommends itself to us particularly for the cheapness with which we are able to build it in our own workshops at the cost of only a few pounds a time.

The difficulties of recording the pressure phenomena of the very first breath of life in a case of normal labour are, of course, considerable and require efficient teamwork which I gratefully acknowledge in my colleagues. Attempts fail more often than not, but we have now been successful in obtaining intelligible readings both at birth and immediately after birth in 40 infants.

An example of a record of the very first breath is shown in figure 3 and of the first cry in figure 4. It will be seen that in the healthy baby these intrathoracic pressure swings are very great as compared with adult respiration. Initial swings in the region of 40 cm of water are common and in vigorous crying we have recorded pressure swings of over 90 cm of water, which is comparable to serious forced voluntary effort on the part of an adult in the presence of an obstruction to respiration such as a hand clapped over the mouth and nose.

This shows how a baby has to fight for breath in the first instance, overcoming its primary atelectasis and the moist cohesion of its alveolar walls. It also emphasizes the importance of liveliness at birth and freedom from all those compli-

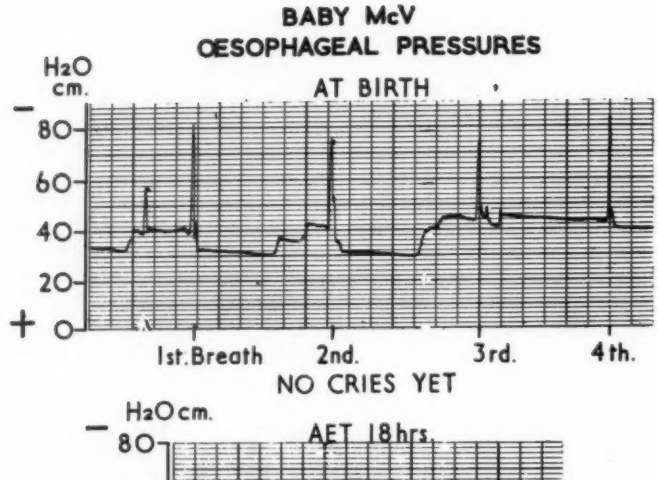

FIG. 3
Pressure changes within thorax on respiration.

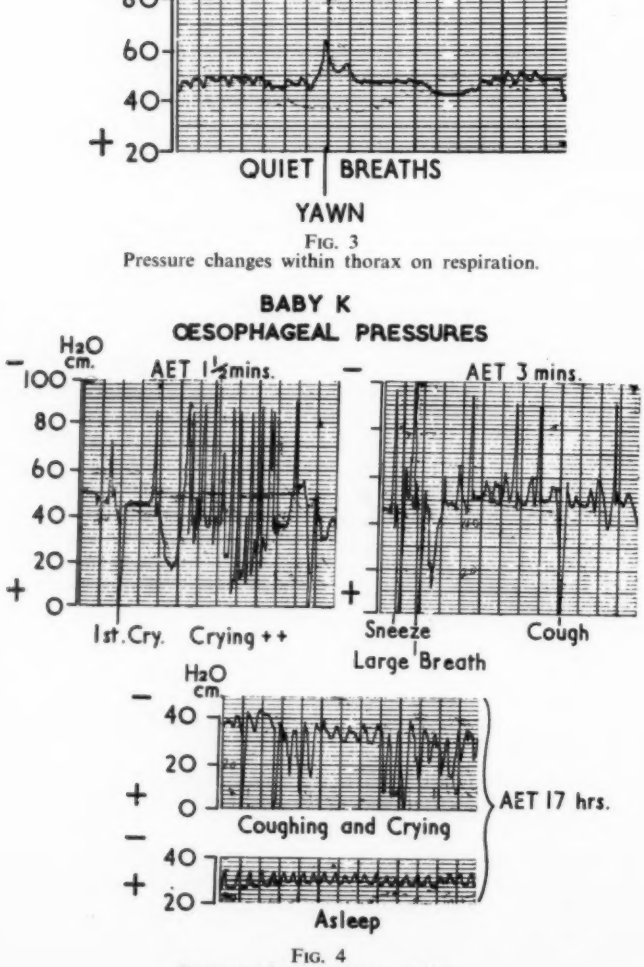

FIG. 4
Pressure changes due to crying.

cating factors, including the persistent and excessive effect of drugs and anaesthetics.

As the lungs are expanded the resistances to breathing become progressively less. This is reflected in the smaller intrathoracic pressure swings now recorded. In other words once the alveoli are opened up it takes much less effort to keep them so.

A well expanded lung is a lung less vulnerable to subsequent pneumonic consolidation and, it is thought, to the complication of hyaline membrane disease.

As Smith and Chisholm (1942) have remarked, the pressures naturally employed to expand the lungs are far higher than one would dare to use with any artificial device for the fear, and certainty, of damaging the alveoli and ducts. The fact that the natural start of breathing so seldom inflicts damage is probably due, as Day et al. (1952) have suggested, to the very brief periods of time over which these pressures act, namely less than 0.15 seconds. We are now contemplating, as the next step, investigating not only the pressures of early breathing but the times over which they act, which should be possible by minor alterations to our existing apparatus.

It has already been explained how the resistances to respiration diminish as progressive aeration of the lungs takes place and how the pressures needed to meet these resistances, that is to say the degree of respiratory effort, become steadily less. In other words, a smaller effort is now rewarded with adequate ventilation and tidal volumes. It appeared desirable, therefore, simultaneously to measure the intrathoracic pressure changes as an index of respiratory effort and the tidal airs as an index of respiratory achievement. In this way we hope to illustrate the degree of lung compliance or the reverse, due, for example, to atelectasis and possibly hyaline membrane.

The underlying theory is that a baby with atelectasis may try hard but get little tidal air result, that a baby with central depression will neither try hard nor ventilate well, and that a healthy baby will achieve a large tidal air corresponding to its pressures of effort, similarly a small tidal volume with low pressures, the ratio of effort to achievement bearing a better relationship than in respiratory disease (fig. 5).

To do this required the development of a suitable spirometer, our next hurdle, especially when one recalls that a premature baby may have a tidal air of only a few millilitres or less.

Our original spirometric technique, using the trip spirometer of our own design (Donald and Lord, 1953), was not suitable for this purpose as it dealt only in minute volumes and we passed the apparatus on to Dr. Hilda Roberts (1957) who carried out a massive survey of neonatal minute volumes with it in relation to analgesic drugs used during labour.

An electronic method was essential in order to match the recordings on a twin channel recorder with the electromanometric results. Up to now we have used a balanced float chamber whose excursions cause a shutter to interrupt, to greater or lesser degree, a beam of light focussed upon a photo-electric barrier cell. The tidal air tracings shown in figure 5 give an example of the results obtained. Although we were able to make these double records in several dozen instances and to show what we were trying to prove, I have constantly disliked this method of spirometry with its rebreathing, its drift, its general unhandiness and its inability to do more than record the widely varying tidal air values, which one gets in neonates without any of the advantages of integration as minute volumes and the averaging out of tidal airs.

After nearly two years work I am glad at last to report that Dr. Greer has produced an integrating spirometer, entirely without float chambers or moving parts, although it is too early yet to evaluate our results with it.

DIFFICULTIES IN MAINTAINING RESPIRATION

More babies who survive the immediate hazards of birth die thereafter from respiratory failure of one type or another than from any other cause, atelectasis in particular being one of the commonest causes of neonatal death.

This atelectasis, moreover, is often secondary inasmuch as it supervenes upon lungs previously known to have been at best partially expanded. Abundant proof of this is easily obtainable by clinical observation. A baby, for example, cannot cry and maintain an adequate degree of oxygenation by its respiratory efforts without having a sufficient number of pulmonary alveoli function-

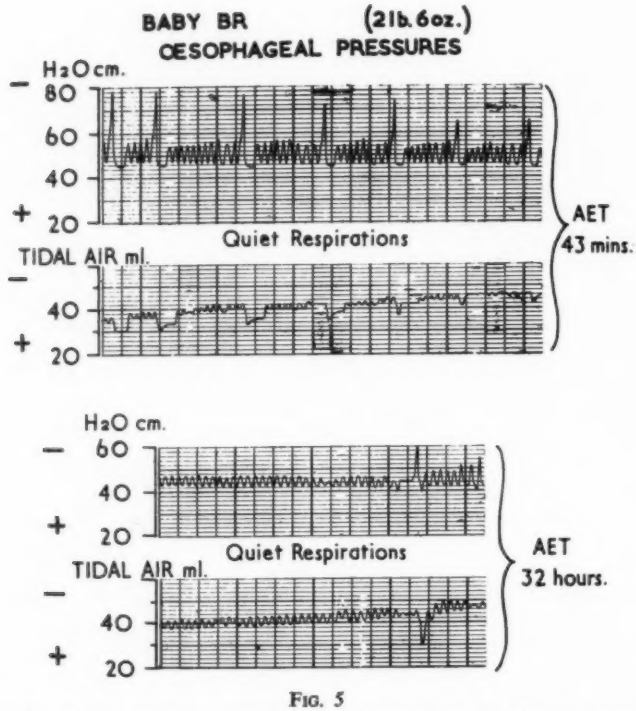

FIG. 5

Falling ratio of oesophageal pressure/tidal air accompanying pulmonary expansion.

ing, and yet it may die with completely solid lungs, showing that it has lost what degree of pulmonary aeration it ever had. Also by spirometry we have repeatedly registered tidal airs which indicated a certain degree of aeration before death from (or with) complete atelectasis. Lastly, pulmonary expansion may be radiologically demonstrable and yet may be seen to deteriorate during life until general radio-opacity develops.

Hyaline membrane. Often associated with the type of secondary atelectasis outlined previously is the interesting pathological phenomenon known as hyaline membrane. The term refers to the appearance, microscopically, of an acidophilic acellular membrane staining pink with eosin, which is to be seen plastered around the walls of a number of alveolar ducts which are often themselves overdistended. Surrounding these are large areas of collapsed alveoli, although it cannot usually be definitely asserted that these alveoli had ever been previously expanded (fig. 6).

It is believed that this membrane owes its peculiar distribution to the mechanical effects of air passing through the alveolar ducts and that the membrane then blocks off the entrances to surrounding alveoli from which contained air is rapidly absorbed, producing what Morison (1952) accurately, if none too euphoniously, describes as secondary resorption nonaeration. This appearance and distribution depend on the child having breathed, at least for a time.

The source of hyaline membrane is not known with certainty and there is much controversy about it. Claireaux (1953) was able to reproduce a facsimile of the condition in rats by injecting intratracheally liquor amnii which had been treated by incubation and inspissation, a process which altered the squames present in the liquor and caused them to lose their nuclei

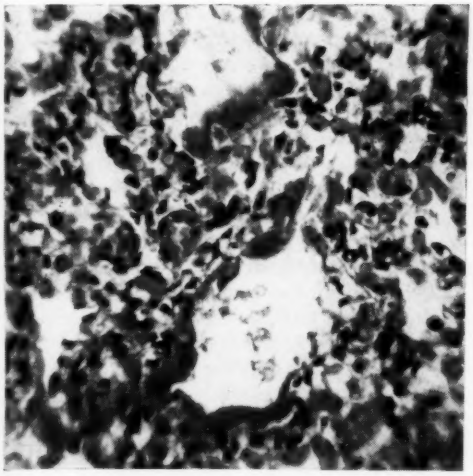

FIG. 6
Hyaline membrane (high power magnification).

and cell outlines. It was suggested that such material formed the basis of the membrane and owed its position, deep within the lungs, to intra-uterine respiration.

The membrane contains a polysaccharide, such as is known to be present both in meconium and squames. Against the theory that the membrane results from changes occuring in the solid constituents of inspired liquor amnii, is the fact that it usually occurs in premature babies who have often suffered no stimulus from asphyxia to inspire deeply in utero, and who may have been simply lifted out of the uterus at a perfectly tidy and well oxygenated elective Caesarean section. Furthermore, some of the worst cases of deep inspiration of liquor amnii and meconium associated with gross foetal anoxia are to be seen in difficult postmature labours and yet, whatever other hazards such a baby has to face, hyaline membrane is not one of them. Hyaline membrane in postmaturity is so rare that Claireaux (1955) was sufficiently interested in finding a case to write and tell me about it.

The other principal theory about the aetiology of hyaline membrane is that it is an exudative phenomenon because a similar histological picture can sometimes be seen in older children with a variety of terminal diseases.

Some pathologists think that this membrane has little if any significance as a direct cause of atelectasis and that its presence is simply incidental, Ranstrom (1953), for example, pointed out that the areas of atelectasis in a section of lung did not necessarily correspond with the areas in which the hyaline membrane could be demonstrated. This, however, is a minority point of view. My own tentative guess is that howsoever the membrane may arise (and it is possible that both main theories are partially correct) its persistence, and therefore its detection at necropsy, depends upon the fact that the pulmonary circulation and vascular bed throughout the lungs have, for one reason or another, been insufficiently opened up, and that the materials which go to form the membrane are not efficiently and quickly enough absorbed as would happen in the presence of an active pulmonary circulation. Witness, for example, the rapidity with which intra-alveolar fluid can be absorbed in a healthy baby's lungs without any need for tracheal aspiration, even if that were much use, which I doubt, in getting rid of deeply inhaled liquor.

When a baby starts breathing and crying vigorously it not only opens up its alveoli but it also opens up the pulmonary vascular bed so that the well-known rearrangements in the circulation within the heart and great vessels at birth take place as a result of the diversion of blood through the pulmonary capillaries. This diversion must surely be due to the negative inspiratory pressures exerted by the baby in its respiratory efforts. This brings us back to where we were before and stresses the enormous value of a vigorous and flying start to respiration. The really lively and active baby at birth, even though seriously premature, is far less likely to develop hyaline membrane disease.

The clinical picture is often characteristic. The baby is frequently premature, though not as a rule excessively so. A higher proportion than usual have been delivered by Caesarean section and the chances of hyaline membrane disease are even higher if the mother is diabetic. It is never found in association with stillbirth.

More often than not asphyxia at birth is not a serious problem and commonly the child breathes and cries fairly well and initially maintains a good pink colour. A false sense of security is

readily encouraged but within the next two hours, sometimes within the next twenty minutes, a careful inspection will show that all is not well. This is often the time when surgeon and anaesthetist are relaxing over a cup of tea, unaware of the disappointment ahead. The first clinical signs of mischief are inspiratory recession of the chest wall, chiefly in the subcostal areas, but as the recession gets worse it includes the intercostal spaces and even the sternum and suprasternal notch. The sign very easily appears in severe degrees of prematurity because of the softness of the thoracic cage but is doubly significant and ominous in more mature babies with tougher ribs.

The recession shows up the resistances to pulmonary expansion which are being faced by the baby. Expiratory grunting can now be heard and as respiratory distress deepens the alae nasi can be seen working.

Usually the baby continues pink in colour and may have short bursts of crying but the usual position adopted is supine with both knees drawn up and with the thighs widely abducted. The arms lie flexed at the elbows with the hands in full supination alongside each side of the head which is turned to one side.

It can be seen that the baby is literally fighting for breath and the effort after a few hours exhausts it so that, without warning, it stops breathing for a few minutes and has its first "blue", or more accurately "grey", attack. Sometimes it dies there and then, but more commonly it starts breathing again or is revived by one means or another and all appears well for a few more hours. But this is just the prelude to a series of grey attacks, in one of which it dies, usually within the first two days of life, sometimes later. Not all such cases end fatally and recovery from the hyaline membrane syndrome as described above is possible, especially in the less severely premature. It is hard to tell for certain which infants will live and which die, but a sequence of more than five grey attacks is very ominous, and even the prospect of survival in such a case is shadowed by fears of how much damage may have been done by anoxia to the central nervous system.

The diagnosis of hyaline membrane has, until recently, been a pathologist's necropsy finding and we have been concerned in making it during life in order to assess prognosis and the value of any treatment adopted. Unfortunately, on clinical grounds alone the diagnosis cannot as a rule be confidently made since a number of other causes of respiratory distress can mimic it; for example, intraventricular haemorrhage, pneumonia, other infections, spontaneous pneumothorax (by no means rare), diaphragmatic hernia, cardiac abnormalities, intrapulmonary haemorrhage, and aspiration of material regurgitated from the stomach, to mention some of the more common conditions in differential diagnosis.

We have found radiography, however, of the greatest help and have described the characteristic radiological signs of hyaline membrane (Donald and Steiner, 1953). Briefly these consist firstly of a diffuse miliary mottling which later becomes coarser and more confluent (fig. 7). Finally, in the case progressing towards a fatal issue, the lungs become completely radio-opaque, even blotting out the cardiac outline. Only the air-filled bronchi can be faintly seen against the background of totally atelectatic lung.

We believe that the earlier stages of the disease, as shown by the first two radiological signs, are reversible but that recovery is impossible once

FIG. 7
"Mottling" associated with hyaline membrane atelectasis.

the signs of radio-opacity are complete. Conversely we consider it most unlikely that a baby, even though very premature, will develop hyaline membrane disease once full pulmonary expansion has been demonstrated radiologically. Again this illustrates the importance of a flying start to respiration.

Among the list of differential diagnoses given previously it will be seen that some will be at once apparent on radiography, such as pneumothorax and diaphragmatic hernia.

The science of treatment of hyaline membrane disease has hardly yet begun. At present there is a sort of routine drill in sick nurseries which covers all respiratory difficulties in the newborn, regardless of their aetiology. This routine consists of humidified oxygen, though not too much, in an incubator, the withholding of feeds, perhaps an antibiotic, an occasional sucking out and sometimes a sedative.

As a practical proposition differential diagnosis has no more than academic interest, but it will become very important indeed if hyaline membrane, for example, can not only be diagnosed during life but can be successfully treated (or prevented).

Intraventricular haemorrhage. Intraventricular haemorrhage has already been mentioned in the differential diagnosis, and in the more premature and smaller weight babies its importance looms hideously large. The pathological lesion is characteristic. As a result of asphyxia before, during or, very commonly, after delivery there is great engorgement of the blood vessels within the brain, one of which, most often in the floor of a lateral ventricle overlying the optic thalamus, ruptures and floods the ventricular system with blood. Grey attacks, as with hyaline membrane, are liable to follow one another until death occurs, usually within the first seven days, although it is sometimes sudden and unheralded. This variety of intracranial bleeding has nothing whatever to do with trauma at delivery but is entirely due to an episode of asphyxia in association with prematurity.

The desirability of survival in the case of a baby so afflicted is sociologically debatable, and any active line of treatment directed against hyaline membrane would not be applicable here. Unfortunately hyaline membrane and intraventricular haemorrhage are often found at necropsy in the same victim. Both conditions are associated with asphyxia, being either cause or effect or perhaps both.

Table I shows the primary cause of death in 99 consecutive cases of neonatal death submitted to necropsy at the Royal Maternity Hospital, Glasgow, and it will be seen that asphyxia, in one manifestation or another, forms the hard core of the neonatal death rate. The one obvious deduction to be made is that asphyxia is to be combated at all times and in all places and it is in response to this principle that I have interested myself for so long in a variety of respirators.

TABLE I

Neonatal deaths: Royal Maternity and Women's Hospital

14 months to February 1956; 99 cases.	
Asphyxia/atelectasis/prematurity ... ... (2 cases of suprarenal haemorrhage) (8 cases of Caesarean section)	42
Intraventricular haemorrhage ... ... (17 cases premature)	23
Tentorial tear	8
Foetal abnormality	14
Haemolytic disease	5
Infections	3
Pneumothorax	3
Pulmonary haemorrhage	1
	99

RESPIRATORS

One can hardly be complacent about the survival rates of premature babies in even the most up-to-date units from the present rather limited routine treatments. Since, from observation, it appeared clear that the babies who died with atelectasis died as a result of asphyxia or physical exhaustion in trying to ventilate their lungs, or from both, we have attempted to lighten their respiratory load by devising a machine that would do some of their breathing for them.

We started at St. Thomas's Hospital with an infant Drinker type of apparatus which, though very flexible as far as pressures and frequency of operation went, had very soon to be discarded when it was noticed that it was impossible to adjust the rate of the machine to the capricious and irregular behaviour of a newborn baby's breathing, especially of one that was in need of

assistance. The baby tended to fight against the set rhythm of the machine so that more harm than good was done and we often observed a state of " protest apnoea " in others.

Clearly, if respirators were going to be of any use at all, they must keep step with the child's respiratory efforts if present and yet be capable of running at a preset rate in the total absence of spontaneous respiratory activity.

A detector mechanism which would trigger the respirator into immediate activity at the beginning of an inspiration was wanted, and our solution was to use a mirrored flap valve in the inspiratory circuit the lifting of which deflected a beam of light focused upon a photoelectric cell (fig. 8), thereby altering its voltage output. Thereafter the rest is simply a matter of technical electronics, the fascinating details of which would be out of place here. Sufficient to say, the final effect is the opening of a valve which allows a sharp change in pressure to be brought to bear upon the baby.

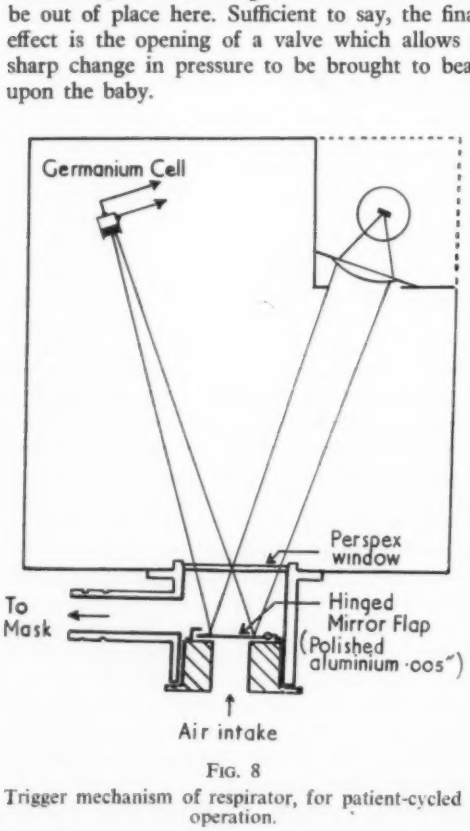

FIG. 8
Trigger mechanism of respirator, for patient-cycled operation.

There are three possible ways of influencing the baby's breathing by pressure changes. The first which we employed depended upon negative extra-thoracic pressure to produce inspiration in a tank type respirator. While I was at Hammersmith Hospital we produced an intermittent positive pressure machine, triggered upon the same principle, which is much handier for short term treatment as the machine works either by a mask or endotracheal tube. The third and obviously attractive method would be the use of a cuirass respirator, but all my experiments with cuirasses to date have been defeated by the infinite variety of shapes and sizes of a baby's chest wall.

Whatever the type of respirator employed it must align itself to assisting rather than opposing the natural breathing efforts of the baby. This principle of simultaneous respiratory assistance has been the subject of a *Lancet* editorial (1953).

Of the three methods of applying augmented respiration, the first, i.e. the tank type, has all the technical difficulties of mounting the baby within it, with very little time to spare. The business of making a neck seal is particularly formidable, since a baby's neck is an unsatisfactory affair having little length and an oblique angle of cross section. The seal must not leak but, on the other hand, must not constrict and it should be capable of withstanding the to and fro piston effect of the pressure changes within the body tank.

Our final method of dealing with this problem was to pour a thick solution of Duplitt (one of the alginates) round the neck and head, omitting the face. The solution was designed to set within about three minutes with a rubbery consistency, conforming exactly to the child's shape as it did so. By then coating the surface of the seal with Tylose, evaporation and disintegration of the seal could be prevented for many hours.

We called this machine a servo respirator and our experiences with it have been published elsewhere (Donald and Lord, 1953; Donald and Young, 1952). What really limits its wider and continuous use is the tremendous difficulty of safely, quickly and satisfactorily mounting a very sick baby within it, a performance usually requiring three people thoroughly practised in the drill.

A respirator capable of working through a mask or endotracheal catheter obviously commends itself because of its simplicity of handling, but it is difficult to keep up the treatment for long periods and its use is more applicable in meeting respiratory emergencies. It is one of these machines which is in current use at the Royal Maternity Hospital, Glasgow.

The problem is how to help a baby to breathe without bothering it to breathe and there is a natural reluctance to employ any mechanical device unless the need for it is obvious and often therefore too late. It is small wonder then that our results are not numerically impressive, since it is "last ditch" treatment. Out of 48 infants treated since coming to Glasgow and since the last series was published, only 16 are alive, the smallest weighing 2 lb 3 oz. It is only fair to point out that of the 32 infants who died, 22 weighed less than 3 lb and of these 15 weighed less than 2 lb, many of them being previable abortions with the smallest only 14 oz in weight.

With these clearly hopeless cases of gross prematurity we were interested to see if we could at least achieve a fair degree of pulmonary aeration with the help of the respirator kept working for long periods through a nylon non-irritant endotracheal tube.

Of four infants so treated, one is alive; another (fig. 9) lived for eight days and died from feeding difficulties. Unfortunately consent for necropsy was refused. The X-rays, however, showed progressive aeration within the first twenty-four hours after which no further respirator treatment was given. A third was a foetus aborted at twenty-two weeks who only lived an hour or so, and the fourth was a previable baby of 27 weeks gestation, weighing 1 lb 12 oz, who was treated off and on for three days in the face of recurrent grey attacks and in whom aeration improved (fig. 10). Thereafter progress was satisfactory until the sixteenth day when the infant suddenly collapsed and died.

At necropsy it was found to have had a severe intraventricular haemorrhage whose existence we had not expected. What was particularly worrying was that the large blood clot was already well organized and firmly adherent to the ventricular walls, signifying that it had been present for a long time, probably following one of the innumerable bouts of asphyxia during the first three days of life.

FIG. 9

Gross prematurity and atelectasis.

It is chastening to reflect that this child came very near to surviving, perhaps thanks to our meddlesome interference and zeal, and it is as well to pause to consider how far this sort of work is worth while.

Our failures have been numerous enough to provide us with plenty of food for thought and we have learnt a great deal. We now know that there is more to living than breathing and that in dealing with atelectasis one may be simply transferring the cause of death in a mortality table from one column into the next. Above all we have now some idea of how much there is yet to learn. It is in this spirit that I venture to submit out tentative conclusions to date.

CONCLUSIONS

(1) Pulmonary aeration is rapid in the normal baby.

(2) Respiratory efforts at birth are very large and compare on measurement with powerful deliberate efforts on the part of a healthy adult.

(3) A flying start to respiration is important.

(4) Atelectasis can be assessed and measured during life.

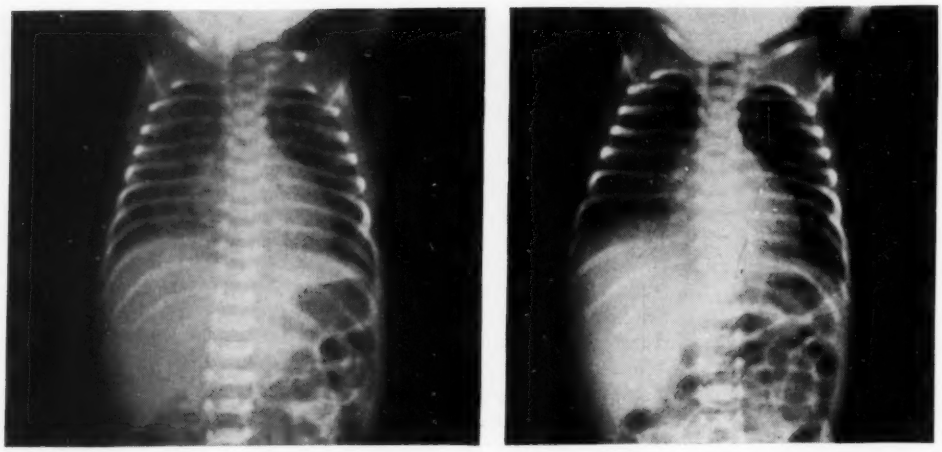

FIG. 10
Progressive aeration. Respirator case. Maturity 27 weeks. Weight 1 lb 12 oz.

(5) Atelectasis is often secondary, steadily progressive and in this instance fatal.

(6) Hyaline membrane need no longer be confined to postmortem diagnosis.

(7) Hyaline membrane produces a sequence of characteristic radiological signs.

(8) Hyaline membrane is reversible in its early stages.

(9) The risk of hyaline membrane is influenced by the circumstances of delivery quite apart from prematurity.

(10) Augmented respiration is safe, logical and more effective than standard techniques of artificial respiration.

ACKNOWLEDGMENTS

This programme of research is being, and for the last two years has been, supported by the Scottish Hospital Endowments Research Trust, whose help is gratefully acknowledged. The Regional Physics Department of the Western Regional Hospital Board has supplied technical assistance in brilliant and boundless measure; in particular I have to thank Dr. Lenihan, Dr. Greer and Mr. MacFadyen.

My own colleagues at the Royal Maternity Hospital, Glasgow, especially Dr. Margaret Kerr and Dr. Ian MacDonald, have done the really hard work and I am glad indeed of their help.

Before coming to Glasgow the work was for three years supported at Hammersmith Hospital by a Leverhulme Research Scholarship awarded by the Royal College of Obstetricians and Gynaecologists, and innumerable instances of help came from sources such as the National Birthday Trust who lent me a carbon dioxide infrared spectrum analyzer. As I look back over the last eight years I feel so amazed at the amount of help I have received from so many people both in medicine and in industry that the task of worthy acknowledgment is beyond hope of fulfilment.

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BOOK REVIEW

Symposium on Anaesthetics Teaching. Organized by the Postgraduate Medical School of London. Edited by Dr. J. P. Payne. Printed by The Shenval Press, London. Pp. 123.

Fundamental changes in the medical curriculum are imminent and many stimulating ideas were ventilated at this symposium which was attended by ninety-three consultants. The subjects covered the problem of postgraduate teaching in pharmacology; the general medical training for anaesthetic specialists; the aims in training the specialist anaesthetist; training in methods of research; the place of anaesthesia in the medical curriculum; the teaching of undergraduates; as well as the special problems of obstetric anaesthesia and the teaching of hypnosis.

In the past the aim of Medical Schools was to educate their students to become general practitioners, but now the trend is to produce a man who is potentially fitted to undertake any of the disciplines of medicine. To provide the undergraduate with all the knowledge he needs is no longer feasible.

It would seem that this specialty has much to offer the undergraduate as a part of his general medical training, and the anaesthetist may soon take an active part in teaching applied basic sciences to undergraduates; at least one scheme of this kind is already in operation. Any doctor ought to be able to resuscitate and to care for the unconscious patient in all circumstances, which may mean that the practice of intubation would have to be taught to undergraduates.

The Primary F.F.A.R.C.S. examination is a major difficulty at the present time. To overcome this it was suggested that more basic science training should be given at the undergraduate level, so that the Primary examination might be omitted at the postgraduate stage when there is little opportunity for learning basic science, because this is the time for acquiring a knowledge of anaesthesia itself.

The papers which were read and the discussions that followed have been gathered together, almost word for word, into a single manual. Unfortunately there is no index. Nevertheless, the symposium is full of interest and it will be a cornerstone for the architects of future anaesthetic training.

R. P. Harbord

Brit. J. Anaesth. (1957), **29**, 570

GAS ANALYSIS BY REFRACTIVE INDEX MEASUREMENT

BY

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Messrs. Cyprane Ltd.

ALL gases and vapours have a specific refractive index and under suitable conditions its measurement can be made quickly and accurately.

In considering the refractive index of gases it is convenient to regard the refractive index, μ, to be the ratio of the velocity of light in vacuo to the velocity of light in the gas such that:

$$\mu = \frac{\text{Velocity of light in vacuo}}{\text{Velocity of light in the gas.}}$$

The velocity of light in the gas will depend on the number of molecules present, that is on its density which will depend on the pressure and temperature. The refractive index will, therefore, also vary with the pressure and temperature, and refractive indices of gases are usually given corrected to 0°C and 760 mm absolute pressure by assuming that $\frac{\mu - 1}{\rho}$ = constant, where ρ is the density.

Refractive indices of some commonly used gases in anaesthesia are given in table I. The refractive index is determined for the sodium D line ($\lambda = 5893 \times 10^{-8}$ cm at 0°C and 760 mm absolute pressure).

TABLE I

Gas	Refractive index
Oxygen	1.000272
Nitrogen	1.000297
Air	1.0002918
Nitrous oxide	1.000515
Carbon dioxide	1.0004498
Chloroform	1.001455
Trichloroethylene	1.001784
Halothane	1.00151 (White light)
Water vapour	1.000257

While absolute measurement of the velocity of light in a medium is difficult, it is quite easy to compare the velocity of light in one medium with the velocity of light in another. A suitable instrument for this purpose is the Rayleigh Interference Refractometer.

This instrument is shown diagramatically in figures 1 and 2. Figure 1 is a plan view showing the components as they appear from above. Figure 2 is a side view of the same arrangement.

Light from the filament of a motor-car headlamp bulb A, is concentrated on a vertical slit C, by the lens B. From the slit C, light passes through the lens D, where the rays are made parallel, the slit C being at the focal point of the lens D. GG_1 are two similar square tubes with

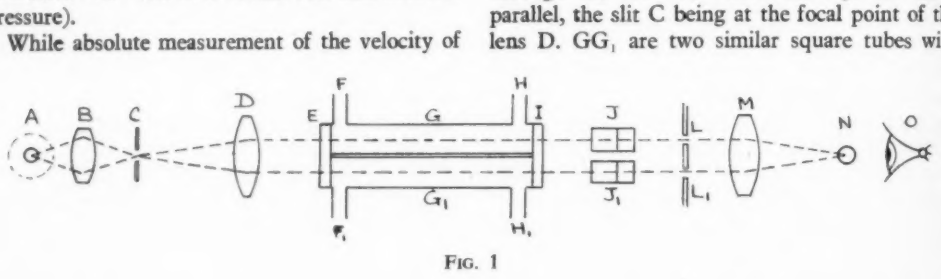

FIG. 1

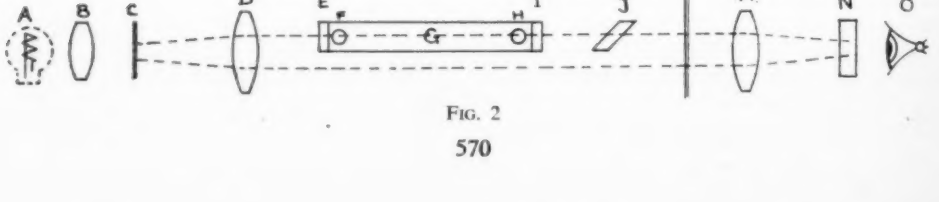

FIG. 2

inlets HH_1 and outlets FF_1. Over the ends of the tubes GG_1 two optically flat glass plates EI are cemented. Both the tubes GG_1 are gastight and do not communicate with each other. One tube is used to contain the sample gas to be analyzed; the other contains a reference gas whose refractive index is known.

The rays of light from D, now parallel, pass through both tubes GG_1 and their cover glasses EI. The rays of light which have passed through the tube G_1 now pass through a fixed sloping glass plate J_1, while the rays which have passed through the tube G pass through an exactly similar plate J, which can be rotated so as to alter the angle of slope compared with the fixed plate, by amounts which can be accurately measured. After passing through the plates JJ_1, the rays pass respectively through slots LL_1, to a lens M, which brings both rays to a focus at N, which is a cylindrical lens, magnifying in the horizontal direction only, where they may be seen by the observer's eye O. Two other beams of light from D pass underneath the tubes GG_1, but not through the glass plates JJ_1, and this light also is observed by the eye at O.

If the light source at A were monochromatic, the observer at O, would see a field as at figure 3. The horizontal black line is the shadow caused by the bottom wall of the tubes GG_1. The vertical black lines B, above the line A, are interference fringes caused by the two beams of light which have passed through the tubes GG_1, and the vertical lines below the line A are interference fringes caused by the beams which have passed underneath the tubes GG_1. The formation of the interference fringes is shown diagrammatically in figure 4. The point A is on the line vertical to and midway between the two slits LL_1, and is therefore equidistant from each slit. Rays of light leaving the two slits are in the same phase; that is a crest leaves L at the same time a crest leaves L_1 and, the distance LA L_1A being the same, will arrive at A also in phase and will reinforce each other causing a bright band.

If the point B, on one side of A, is such that the distance LB is one wavelength less than the distance L_1B, the two rays will again reinforce and cause another bright band. Midway between A and B, at C, the difference in path LC—L_1C, will be half a wavelength and the two rays will always arrive out of phase; that is a crest of one wave will arrive at the same time as the trough of another and they will extinguish each other, causing a black band. The eye looking through the lens N of figures 1 and 2 will therefore see a series of bright and dark bands.

If now the gas in tube G_1 is replaced by a gas of different and slightly greater refractive index from that in tube G, the light which passes through tube G_1 will be retarded, and the rays arriving at the central point A (fig. 4) will no longer be in the same phase at that point. They will be in phase with a ray from L, which has taken longer to reach the lens N (figs. 1 and 2), e.g., at point D (fig. 4). The same reasoning applies to all the interference bands so that the observer will see all the bands above the line A (fig. 3) move over to the left.

The bands below the line A (Fig. 3) have been unaffected by this change of refractive index and stay in their original position.

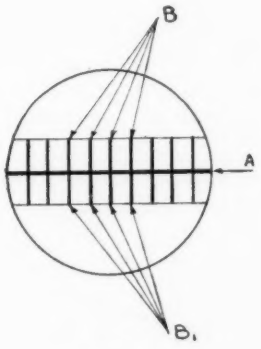

FIG. 3

If the source A (figs. 1 and 2) is not monochromatic but is white light, instead of seeing a field as figure 3 one will see the field as figure 5. On each side of the central bright fringe two well defined black fringes, BB_1, will be seen. The next pair of dark fringes, CC_1, will be less well defined and further fringes will be hardly visible. The field tails off on each side in spectrum colours. The different wavelengths comprising white light cause interference fringes at different distances

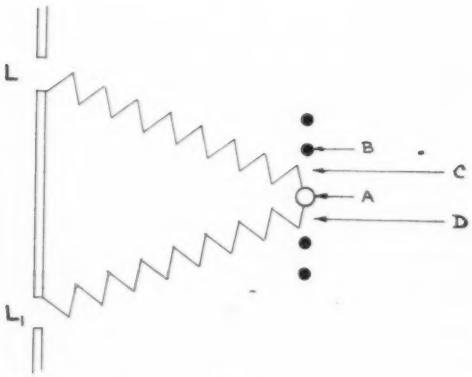

FIG. 4

from the axis and it is only the two central black bands which are clearly defined.

Using white light, when the refractive index of the gas in tube G_1 (figs. 1 and 2) is increased, the two bands B (fig. 5) move to the left, the two bands B_1 again are unmoved. By suitably rotating the glass plate J, so that a greater thickness of glass is interposed, the light which has passed through the reference gas tube G, can be retarded by the same amount as the light passing through tube G_1, and the lines B (fig. 5) brought back and matched up with the reference bands B_1 (fig. 5).

If means are provided for measuring the amount of rotation of the glass plate J one can calibrate this rotation against refractive index change or against the percentage of one gas in the reference gas.

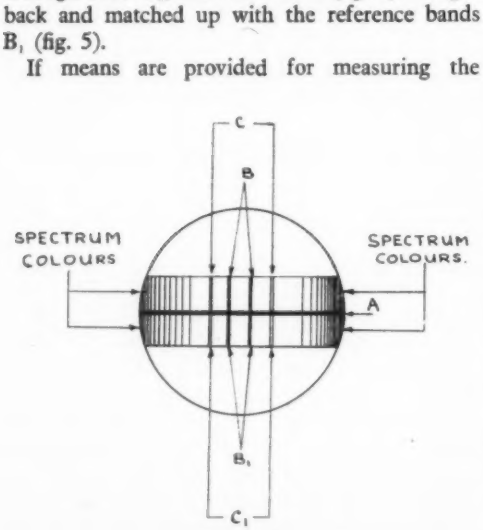

FIG. 5

To calibrate in terms of refractive index change, a monochromatic light source, such as a sodium lamp, must be substituted for the motor-car lamp A (figs. 1 and 2). With air in both tubes the black bands in figure 3 are aligned and a reading taken on the dial indicating the amount of rotation of the glass plate J (figs. 1 and 2). By moving the dial the bands above A (fig. 3) are moved over one band and again brought into alignment and a reading taken. This is repeated for several succeeding bands and the dial reading plotted against the number of bands. The refractive index change ($\delta\mu$) which is equivalent to the movement of the dial for one band is:

$$\delta\mu = \frac{\lambda}{L} = D.$$

Where $\delta\mu$ is the equivalent refractive index change, λ is the wavelength, in centimetres of light used.

L is the length of the tubes GG_1 (figs. 1 and 2), again in centimetres.

D is the dial reading for the movement of one band.

In using a calibration, derived from monochromatic light, when white light is used there is theoretically some error, but this appears to be small for practical purposes.

The refractometer can be calibrated, e.g., for nitrous oxide and oxygen, by mixing up known volumes of the two gases to give a series of known mixtures, then passing the known mixture through the tube G (figs. 1 and 2) while pure nitrous oxide is passed through tube G_1 (figs. 1 and 2). A pure sample of nitrous oxide can be prepared by opening the valve of a nitrous oxide cylinder (held vertically) and very rapidly discharging from the gas phase until the cylinder is covered with frost and the gas is issuing only gently.

The sample flow passed through the tubes GG_1 (figs. 1 and 2) should not be large enough to cause an increase in pressure in the tubes GG_1 (figs. 1 and 2) or a false reading will be obtained.

For calibrating the instrument for vapours one can volatilize a known weight of the liquid, e.g.,

trichloroethylene, into a known volume of the known gas, such as air. The volume-to-volume percentage of the resultant mixture can be calculated from the vapour density of the trichloroethylene. Precautions must be taken to ensure thorough mixing. Apparatus to do this calibration accurately would be rather cumbersome and the technique laborious.

Where the vapour pressure of the liquid is known (and this is easy to measure with accuracy) a simple method is to generate the known mixture by bubbling the reference gas through the liquid held at constant temperatures, and to pass the resulting mixture through one tube while the reference gas is passed through the other.

If the vapour pressure is p and the barometric pressure P, the volume-to-volume percentage will be:

$$\frac{p}{P} \times 100 \text{ per cent}$$

The whole of the saturating vessel should be of glass, since rubber can absorb most anaesthetic vapours and can also give out any vapours with which it has been in contact. The connection from the saturating vessel to the refractometer should also be of metal or glass, though it is possible to use a rubber tube as a sleeve joint.

The temperature required for most anaesthetic liquids to give a concentration in the range used in anaesthesia is usually below zero Centigrade, and the saturating apparatus can conveniently be immersed in alcohol or trichloroethylene cooled with solid carbon dioxide. A wide mouthed thermos jar is useful for containing the cooling liquid and it will hold a steady temperature long enough to make the necessary readings. If at a given temperature a steady reading can be obtained over a range of flows of the order of 10 to 1, it can be assumed that the saturator is giving 100 per cent saturation.

Having found the calibration constant of the instrument for two gases of known refractive index, it is possible to calculate—with reasonable accuracy—the constant for two other gases if their refractive indices are known.

For example, suppose that the refractometer dial reading with carbon dioxide in one tube and nitrous oxide in the other is 0.420 at 15°C and the barometric pressure is 740 mm Hg, the calculation is continued as follows:

The refractive index of nitrous oxide at 0°C and 760 mm Hg	= 1.000515
The refractive index of carbon dioxide at 0°C and 760 mm Hg	= 1.000450

Correcting to 15°C and 740 mm Hg:

The refractive index of nitrous oxide at 15°C and 740 mm Hg	= 1.000475
The refractive index of carbon dioxide at 15°C and 740 mm Hg	= 1.000415
The refractive index difference at 15°C and 740 mm Hg	= 0.000060

A dial reading of 0.420 = a refractive index change of 6×10^{-5}. Therefore a refractive index change of 1.0 = a dial reading of

$$\frac{0.420}{6} \times 10^5$$

$$= 7.0 \times 10^3$$

To find the calibration constant for nitrous oxide in oxygen.

The refractive index of nitrous oxide at 15°C and 740 mm Hg	= 1.000475
The refractive index of oxygen at 15°C and 740 mm Hg	= 1.000252
Difference in refractive index	= 0.000223

$$= 2.23 \times 10^{-4}$$

The dial reading for nitrous oxide in one tube and oxygen to the other would therefore be:

$$2.23 \times 10^{-4} \times 7.0 \times 10^3 = 1.561$$

In the case of nitrous oxide–carbon dioxide one must multiply the dial reading by $\frac{100}{0.420}$ = 238 to convert a dial reading to percentage of nitrous oxide in carbon dioxide.

In the case of nitrous oxide–oxygen one must multiply the dial reading by $\frac{100}{1.56} = 64$ to convert a dial reading to percentage of oxygen in nitrous oxide.

Correction to the refractometer constant for barometer pressure and room temperature can be

made by the formula:

$$K_{t_1 p_1} = K_{t_2 p_2} \times \frac{T_1}{T_2} \times \frac{P_2}{P_1}$$

Where $K_{t_1 p_1}$ is the constant at temperature T_1 and pressure P_1 and $K_{t_2 p_2}$ is the constant at temperature T_2 and pressure P_2.

The inlet and outlet passages FF_1, HH_1 and the tubes GG_1 (figs. 1 and 2) are too small to pass large flows without building up back pressure, so that it is usually necessary to draw only a fraction of the gases requiring analysis through the refractometer tube.

This requirement brings in the possibility of sampling errors. The gases from which the sample is withdrawn must clearly be thoroughly mixed. Little trouble is encountered with gases, but with vapours which are very dense compared with air or oxygen, a spiral strip, or baffle system, may be required to ensure mixing before sampling.

While the refractometer method is rapid and accurate for a mixture of two components, or a mixture of three if the ratio of two of them is constant (i.e., air), it is of limited use in analyzing an anaesthetic mixture such as is commonly given.

Even a mixture like nitrous oxide-oxygen-ether would be difficult to analyze with accuracy since any absorbent used to remove the ether would also remove some nitrous oxide. If, as is usually the case, nitrogen, carbon dioxide and water vapour are also present, the analysis becomes virtually impossible.

Such a mixture would be difficult to analyze by any method and it will probably be necessary to wait for the invention of apparatus for the specific analysis of individual gases, such as the magnetic susceptibility apparatus for oxygen and the infrared analyzer for carbon dioxide, before the problem can be satisfactorily solved.

BOOK REVIEW

Venous Return. By Gerhard A. Brecher. Published by Grune and Stratton, New York and London, 1956. Pp. 148; illustrated. Price 48*s*.

The venous return has always been something of a problem to the anaesthetist who spends time in measuring arterial pressures and in considering their significance. But the heart can only expel as much as it receives, and Brecher's monograph on "Venous Return" explains in masterly fashion the importance of this part of the circulatory dynamics.

The section on methods for venous flow measurement contains an account of the high fidelity electronic bristle flowmeter which was used to study venous return directly. Much of the work has been performed on dogs.

Anaesthetists will be particularly interested in the sections on the respiratory pump, the effect of artificial respiration on venous return, and on the venous return during cardiac surgery.

The monograph contains an extensive bibliography and all of the 55 illustrations are carefully designed and clearly executed. No progressive anaesthetist can afford to be without this excellent work.

R. P. Harbord

Brit. J. Anaesth. (1957), **29**, 575

THE EVOLUTION OF ANAESTHESIA

BY

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(*Continued from Vol.* 29, *page* 291)

THE history of anaesthesia is a large subject; paradoxically, it is also true that it does not exist at all. Anaesthesia is merely a branch of medicine, and its history can only be understood by examining the whole subject. Equally, medicine is a branch of science, while science is but one facet of human activity; it follows, therefore, that the history of anaesthesia can only be interpreted correctly by viewing it in the perspective of other human activities, medical, scientific and social; inventions, discoveries, wars, religious beliefs, and all the manifestations of art and culture.

F. The Pre-Anaesthetic Era (1754–1846).

This period of just under a century saw tremendous changes in the organization of the polity of Western Europe, in the habits and manner of thought of the people, so that, at the end of this period, we unmistakably enter upon a scene familiar to us in almost every particular. The preceding three centuries had seen the marshalling of the forces which, now prepared, were to sweep away the last remnants of medievalism, and found a system of life bound, not upon agriculture and feudalism, but upon science, industry and democracy.

The loss of the American Colonies and the outbreak of the French Revolution practically coincided. The Napoleonic Wars which followed excluded British trade from the Continent of Europe, but the result was only to make Britain stronger and more resourceful. The conquest of India and Canada and the colonization of Australia led to an extension of trade, the more so because Britain had been forced to concentrate on naval rather than land forces. The prosperity which came in the wake of trade was necessarily unevenly distributed, but all classes benefited to some extent, and this was reflected in a tremendous increase in population which rose from about 8,000,000 in England and Wales in 1754 to about 17,000,000 in 1846. Meanwhile, the flow of people to the towns as a result of the increasing mechanization of industry brought about the industrial Revolution. Similar changes, of course, occurred elsewhere, but Britain's grip on the seas and Napoleon's on the land, delayed the development of the Continental countries, so that Britain's pre-eminence was assured, while the invention of the steam-engine and its adaptation to locomotives and steamships revolutionized transport and greatly influenced both mental and material growth.

Liberalizing influences were everywhere at work, not only in politics, but in Art and Religion as well. It is no accident that the final extinction of the Holy Roman Empire occurred only fifteen years after John Wesley's death. In literature, the work of Samuel Johnson, Kant, Goethe, Burns, Scott, Wordsworth, Byron and Shelley falls within this period; in art, Constable and Turner, in music, Mozart, Haydn and Beethoven; while public consciousness of the importance of art was revealed by the opening of the British Museum and the Royal Academy of Arts. The culminating political event was the passing of the Reform Bill in 1832.

In science, the work of such men as Priestley, Lavoisier, Cavendish, Galvani and Volta laid the foundations for the achievements of Thompson (Count Rumford), Humphry Davy and Michael Faraday, and the work of all these was united by close bonds with political, economic, religious and medical thought. In medicine, the power of diagnosis was greatly assisted by the discovery of percussion by Auenbrugger and of stethoscopy by Laennec, while the study of disease was advanced by John Hunter with his interest in comparative and morbid anatomy, and by Cullen

who greatly influenced medicine, not only in Edinburgh, but also on the American Continent. Obstetrics were revolutionized by William Smellie and William Hunter; James Lind had opened the door to the study of vitamins; physiology was advanced by Sir Charles Bell's discovery of the separate sensory and motor functions of the posterior and anterior nerve roots; and surgical skill reached a great height in the hands of Liston.

However, for its immediate results, the most important therapeutic discovery of the period was the introduction of vaccination by Edward Jenner. The mortality from smallpox was enormous, and the publication of Jenner's *Inquiry into the Causes and Effects of Variolae Vaccinae* in 1798 disclosd a safe way to save countless lives. So important was the discovery deemed that Parliament voted Jenner a reward of £10,000, later supplemented by a further £20,000. Among all the benefactors of mankind, Jenner's name must stand high on the list.

Until the War of Independence, medicine on the North American Continent was mainly a pale shadow of British medicine, but with political separation came scientific and medical independence: the Medical School at Philadelphia was founded in 1765, and others followed, the Harvard Medical School being opened in 1783. Greatly influenced by the Edinburgh school, American medicine quickly grew to full stature and began to break new ground, particularly, for example, when in 1809 Ephraim McDowell successfully removed an ovarian tumour weighing 22½ lb., this being almost the first time in which the peritoneal cavity had been invaded by the surgeon. Knowledge of the physiology of digestion was much advanced by the work of Beaumont (1825–1833) on his patient, Alexis St. Martin, who was suffering from a gastric fistula caused by a gunshot wound; and in 1843 appeared an essay *On the Contagiousness of Puerperal Fever* by the doctor and man of letters, Oliver Wendell Holmes.

Of considerable importance in the development of both psychology and anaesthesia was the work of Franz Anton Mesmer (1734–1815). At first working with magnets, and later using the " animal magnetism " which, he believed, flowed from his own body, Mesmer developed a system of therapy, first in Vienna and later in Paris, which had many adherents. In 1784, a commission appointed by Louis XVI, which comprised such famous men as Dr. Guillotin, Lavoisier, Bailly and Benjamin Franklin, reported that no evidence of " animal magnetism " was to be found and that Mesmer's results were entirely due to imagination. Mesmer's treatment consisted of bringing his patients into hysterical convulsions; it was a follower of his, de Puységur, who discovered hypnotic somnambulism, otherwise the mesmeric trance.

Paradoxically the discoveries of the century under review had destroyed the confidence of the public in its doctors, and the doctors in themselves. The old humoral theory of disease had been swept away, and there was nothing to replace it. In the face of disease, the doctors, knowing their ignorance of the cause, were helpless, and there arose, both within and without the field of orthodox medicine, theorists and quacks who attempted to reduce all therapy to simple terms, such as John Brown of Edinburgh, whose theory was that all diseases were sthenic (i.e., caused by over excitation) or asthenic (i.e., caused by under excitation). The former were to be treated with opiates and the latter by stimulants. Such theories led nowhere and merely weakened the power of the profession by promoting feuds and discords among its members, each championing his own futile system, claiming successes which were often exaggerated for his own method, and denying success to his rivals.

With all the great changes in way of life during this period, an even greater change in the habit of thought was taking place; the idea of humanity was beginning to blossom and bear fruit. It may be that the carnage of the Napoleonic Wars and the frightful conditions in the towns which accompanied the Industrial Revolution caused a change in men's hearts. However that may be, the change disclosed itself in many ways, such as the abolition of the Slave Trade (1807), the founding of the Humane Society, the passing of Acts against bull-baiting and bear-baiting and cock-fighting, and the great reduction in the number of crimes for which a capital punishment could be inflicted. Meanwhile, conditions were improved in lunatic asylums and prisons, and the great and

rewarding advances in Public Health were set on foot by Chadwick and Southwood Smith. In the field of medical teaching, the passing of the Anatomy (Warburton's) Act and the licensing of schools of medicine in Britain brought about a great improvement in the standard of teaching and released the teachers from co-operation with body-snatchers.

It was only to be expected that this humane interest in the welfare of others which characterized the early years of the 19th century would soon extend itself to surgery, and that a demand for surgical anaesthesia would soon be felt; accordingly, we find that efforts in this direction were made by an increasing number of people at this time. Thus, in 1807, Baron Larrey rediscovered refrigeration anaesthesia, when he noticed that soldiers who had lain some time in the snow felt no pain during amputation; in 1821, Récamier used hypnotism during cauterization; in 1829, Cloquet successfully amputated a breast while the patient was in a mesmeric trance; in 1832, Wardrop employed bleeding to syncope for a surgical operation; and in the early 1840s, Esdaile in India and Elliotson in London were advocating and practising hypnotism during surgical operations.

It is not to be thought that all these advances occurred easily or without opposition. Every advance was opposed, often with violence, whether in the field of politics or of medicine. Thus, Elliotson was rewarded for his efforts to produce painless surgery by being branded as a quack and driven from his teaching post at University College Hospital.

In 1754, the year in which the pre-anaesthetic era may be said to have begun, Joseph Black announced the discovery of carbon dioxide, and also laid the foundation of the atomic theory by showing that a given weight of calcium carbonate always yielded a definite quantity of carbon dioxide, which could, in turn, be united with calcium hydroxide to form the original quantity of calcium carbonate. In 1772, Joseph Priestley discovered nitrous oxide, and a few years later both he and Scheele announced the isolation of oxygen (dephlogisticated air).

The work of Black, Priestley, Lavoisier and Laplace brought gases very much to the notice of the public. Early in 1799, Dr. Thomas Beddoes opened the Pneumatic Medical Institution at Bristol, with the young Humphry Davy as superintendent. Davy had already experimented with nitrous oxide, and, in 1800, he published his suggestion that nitrous oxide might be used with advantage during surgical operations. The advice fell on deaf ears.

In 1824, Hickman published *A Letter on Suspended Animation,* in which he advocated anaesthesia with carbon dioxide and, in 1828, he applied, through King Charles X, to the Royal Academy of Medicine of France. Hickman's proposal received no support, which was probably as well, since his method of anaesthesia was indubitably dangerous.

As early as 1795, Richard Pearson was advocating the inhalation of ether in the treatment of phthisis, and in the succeeding years both ether and nitrous oxide were inhaled from time to time on account of their intoxicating effects, especially in the U.S.A. These experiences led to the use of both ether and nitrous oxide as anaesthetics, first in 1842, when Clarke gave ether to a patient while Elijah Pope extracted a tooth, and when Crawford W. Long used ether on several occasions for minor surgery. Neither Clarke nor Long published his experiences. In 1844, Horace Wells used nitrous oxide for dentistry, but a demonstration arranged at the Massachusetts General Hospital proved unconvincing. It was left to a former partner of Wells, one William Thomas Green Morton, to demonstrate anaesthesia with ether, which he did at the hospital where Wells had failed, and, from that day, October 16, 1846, the "deepest furrow of the wrinkled brow of agony has been smoothed for ever".

1749–1832. Goethe.

1754. Joseph Black's M.D. thesis. *De Magnesia Alba,* announces the discovery of carbon dioxide, and, by establishing a quantitative basis for chemistry, paves the way for the atomic theory. His paper was first published in 1756, and appeared in book form in 1777 and 1782.

1754. Benjamin Pugh describes an "air-pipe" for the resuscitation of the newly born. It was made of a wire spring, 10 inches long covered with thin, soft leather, and was to be introduced into the infant's mouth digitally "as far as the larynx".

1755. John Hunter (1728–1793) conducts experiments on artificial respiration on dogs by means of a double acting bellows, one chamber of which filled the lungs with fresh air, while the other exhausted the lungs and discharged the "mephitic" air into the atmosphere. The bellows became popular for resuscitation of the apparently dead. Hunter's contributions to surgery, dentistry and medicine were outstanding. His name is intimately associated with the Royal College of Surgeons of England.

1756–1763. The Seven Years War: Frederick of Prussia beats France in Europe; and Britain wins India and North America.

1756–1791. Mozart.

1757. Pitt in power. Plassey.

1759. Quebec, Minden.

1759. British Museum opened.

1759–1796. Robert Burns.

1761. Leopold Auenbrugger (1722–1809) publishes his *Inventum Novum*, in which percussion is described, and the various differences in sound caused by hydrothorax, enlarged heart, etc., are pointed out. No notice of the invention was taken until Corvisart republished the *Inventum Novum* in 1808.

1761. Giovanni Battista Morgagni (1682–1771) publishes his *De Sedibus et Causis Morborum*, which has earned him the title of the Father of Pathology. It was translated into English in 1769.

1763. James Boswell becomes the faithful follower of "The Great Cham", Dr. Samuel Johnson (1709–1783).

1765. Foundation of the Medical School of Philadelphia.

1766. Cavendish (1731–1810) discovers hydrogen.

1768. Foundation of the Royal Academy of Art. The inventions of Watt, Arkwright and others begin the era of manufacturing industry.

1770–1850. Wordsworth.

1770–1827. Beethoven.

1771–1832. Sir Walter Scott.

1772. Prussia, Austria and Russia begin dividing Poland.

1772. Joseph Priestley (1733–1804) discovers nitrous oxide, which he names "dephlogisticated nitrous air". The exact date of the discovery is not recorded, but the experiments which Priestley describes are related to 1772 or, at latest, the early part of 1773 (vide *Experiments and Observations on Different Kinds of Air*, 2nd edition, 1775). He first produced oxygen ("dephlogisticated air") in 1771, but left his invention of this gas unfinished until 1774–5; Scheele also discovered oxygen independently at about this time (1772), his discovery being published in 1777 (*Chemische Abhandlung von der Luft und dem Feuer*, Upsala). Priestley also discovered other gases, notably nitric oxide and methane. Priestley, a Unitarian Minister, a friend of Benjamin Franklin, was of pronounced liberal opinions, and sympathetic to the French Revolutionaries. He received much encouragement and protection from Lord Shelburne, but in 1794 he felt it advisable to emigrate to America on account of the hostility of the "rascal multitude".

1773. Foundation of the Medical Society of London.

1773. Publication of *A Collection of Authentic Cases Proving the Practicability of Recovering Persons Visibly Dead by Drowning, Suffocation, etc*, by Alexander Johnson. The book contains a short account of a "Society for the Recovery of Drowned Persons", founded in Amsterdam in 1767, and focused attention on the practicability of resuscitative measures.

1774. Foundation of the Humane Society (later the Royal Humane Society).

1774. William Hunter (1718–1783), brother of John Hunter, publishes *The Anatomy of the Gravid Uterus*, of which the excellence of the illustrations has never been equalled, either for accuracy or artistic merit. Hunter's name is associated with the Museum which he bequeathed to the University of Glasgow.

1775–1861. Turner, landscape painter.

1776. The Abbé Fontana publishes a work on nitrous oxide and oxygen. In 1779, he described a method of carbon dioxide absorption using "quick lime water", which is mentioned by Ingenhousz (1779). Fontana also contributed substantially to the understanding of South American arrow poisons.

1776. William Cullen (1710–1790) recommends the inflation of the lungs of drowned or suffocated persons by bellows; the first volume of his *First Lines on the Practice of Physick* appears. Cullen, whose interest in the natural history of disease was great, was one of the foremost teachers at Edinburgh. His interests were wide: in 1755 he conducted experiments on the freezing of small animals as a method of producing suspended animation.

1777. Publication of *Expériences sur la Respiration des Animaux* by Antoine Laurent Lavoisier (1743–1794). He was the first to observe the true nature of oxidation and realized that air which had been breathed resembled air which had been used for the oxidation of metals, with the addition of carbon dioxide. He renamed Priestley's dephlogisticated air "oxygéne", because he thought it to be a constituent of all acids. He was executed by the Revolutionaries as an enemy to France ("The Republic has no need for scientists").

1778. John Brown (*c.* 1736–1788), originator of the Brunonian System (vide ante), publishes his *Elementa Medicinae*.

1779. John Ingenhousz discovers ethylene, and publishes the first edition of his *Experiments upon Vegetables*. He proved that green plants utilize carbon dioxide and give off oxygen in sunlight: he was the first to appreciate that breathing is necessary for all living organisms, and that the carbon in plants comes from the air, not from the soil. At the end of the preface of the *Experiments*, he wrote, "When this book was entirely printed, and nothing but the latter end of the preface unfinished, I was informed by my friend the Abbé Fontana, that he discovered a few days ago a new method of pro-

curing to a sick person the benefit of breathing any quantity of dephlogisticated air at a cheap rate." He goes on to describe the use of a solution of quicklime for this purpose, one of the earliest accounts of carbon dioxide absorption ever published. Scheele had also used "milk of lime" for absorbing "fixed air" from the atmosphere in which he kept bees alive by means of his "fire-air" (oxygen). Priestley was unable to confirm the results of Ingenhousz and Scheele.

1779. Publication of *A Medical Commentary on Fixed Air* by Matthew Dobson, the first book on the medical uses of carbon dioxide and carbonates.

1779. Publication of the *Mémoire sur la Découverte du Magnétisme Animal* by Franz Anton Mesmer (1734–1815) Born near Lake Constance, Mesmer qualified in 1766 and practised at first in Vienna where he was friendly with Mozart. His mystical outlook and the quackish nature of his claims caused him to remove to Paris, where his treatment soon became popular. "Mesmerism" consisted in causing hysterical convulsions: the somnambulistic trance, later to be used as a form of surgical anaesthesia, was the discovery of one of Mesmer's followers, de Puységur. In 1784, a commission of distinguished persons, including the celebrated Dr. Guillotin, Benjamin Franklin, and Lavoisier, appointed for the purpose by Louis XVI, reported that there was no scientific basis for Mesmer's claims and that his results were due to imagination. The scientific basis of Mesmerism was to be established by James Braid (vide 1843).

1870. The French Revolution: its anarchy leads to the despotism of Napoleon; it brings great social changes in Europe.

1780. *Observations sur le Magnétisme Animal* by d'Eslon, who was Docteur-Régent de la Faculté de Médecine of Paris, and was Mesmer's most devoted pupil and admirer.

1780. Chaussier of Dijon advocates a special mask and bag of chamois leather for performing artificial respiration on newborn babies. He advocates the use of oxygen.

1781. Appearance of Immanuel Kant's (1724–1804) great work, *The Critique of Pure Reason.*

1781. Henry Cavendish (1731–1810), who had prepared hydrogen in 1766, demonstrates that the combustion of hydrogen and oxygen produces water.

1781. The Abbé Fontana proves that curare affects the "irritability" of muscles without affecting the heart (*Traité sur le Vénin de la Vipère et sur les Poisons Américains"*.

1783. Britain acknowledges the independence of the United States.

1783. Foundation of the Medical Institution of Harvard University through the efforts of Dr. John Warren, its first Professor of Anatomy and Surgery.

1783. Von Schreber writes the first botanical account of American arrow-poisons (*Ueber das Pfeilgift der Amerikaner in Guiana*). He believed that the principal ingredient of "Woorara" (curare) was Strychnos.

1783. De Gardanne issues his *Catéchisme sur les Morts Apparents dits Asphyxiés*, an early essay on the treatment of the apparently dead.

1784. Laplace (1749–1827) publishes his epoch-making *Théorie des Planètes.*

1784. James Moore, brother of Sir John Moore of Corunna fame, describes *A Method of Preventing or diminishing Pain in Several Operations of Surgery.* The method consisted of a sort of vice which could be screwed on to the limb, compressing the main nerves. It was used at St. George's Hospital by John Hunter, but this revival of a method employed by Paré never became popular.

1785. Introduction of the use of digitalis by William Withering (1741–1799).

1786. Desgranges of Lyons describes a pump for artificial respiration.

1788. The colonization of Australia begins.

1788–1824. Lord Byron.

1788. Edmund Goodwin advocates inflation of the lungs of drowned persons by means of Nooth's pump, which later became popular; he also advised oxygen in preference to common air. His book, *The Connexion of life with Respiration* received the gold medal of the Humane Society.

1788. Charles Kite of Gravesend makes the first endotracheal tube ("an instrument to pass beyond the glottis") and describes it in his *Essay on the Recovery of the apparently Dead.* He also mentions the introduction of the tube through the nose, writing "the crooked tube bent like a male catheter, recommended by Dr. Munro, and mentioned by Mr. Portal, Mr. le Cat, and others, is to be . . . introduced through the mouth, or one nostril, into the glottis, when, on blowing through the mouthpiece, or applying the bellows the lungs will be dilated." The reference to Dr. Munro cannot be identified, but it may be to Alexander Munro, primus of Edinburgh, who apparently advocated the inflation of the lungs by artificial means as a method of resuscitation. Antoine Portal (1742–1832) advocated intubation by tracheotomy, but only as a last resort. Claude Nicolas le Cat (1700–1768) expressed a desire to see a tube designed which could be passed through the glottis to assist in artificial respiration (vide *Brit. J. Anaesth.* (1951), **23**, 239).
Kite's *Essay*, which received the Humane Society's silver medal is notable also for the advocacy of the use of oxygen in resuscitation and for the observation that the diaphragm can be stimulated by "throwing a strong galvanic current" across the chest.

1789. Benjamin Rush (1746–1813) is appointed Professor of Physic at Pennsylvania. Rush, one of the great systematists, who sought to simplify the theory of disease and, consequently, treatment, was easily the most famous American physician of this period.

1789. Hans Courtois of Tournai invents a double pump for the ventilation of the lungs through a tracheotomy cannula.

1791. Haydn (1732–1809) visits England, where he is acclaimed.

1791. Luigi Galvani (1737–1798), professor of surgery and anatomy of Bologna, publishes his *De Viribus Electricitatis in Motu Musculari Commentarius*, in which he showed that electricity could be generated in animal tissues.

1792. James Curry, who qualified at Edinburgh in 1784 and who became a physician at Guy's Hospital, publishes his *Popular Observations on Apparent Death and Drowning*. He had already designed an endotracheal tube (1791), similar to Kite's, and he now described additional instruments which also seem to be based on those which Kite described. (He is not to be confused with James Currie, the celebrated hydrotherapist and editor of the works of Robert Burns.)

1794. Erasmus Darwin (1731–1802), grandfather of Charles Dawin, in his *Zoonomia*, suggests blood transfusion for the treatment of nervous and putrid fevers. His offer to transfuse a person dying from "an entirely impervious throat" is interesting for the ingenuity of the method which he proposed (see Keynes, *Blood Transfusion*, Bristol, John Wright (1949), p. 19).

1794. Thomas Beddoes (1754–1808), a Shropshire man, received his M.D. at Oxford in 1786. A friend of Lavoisier, he was forced to resign his post at Oxford on account of his liberal political opinions. He established the "Pneumatic Institute" at Clifton, for the treatment of diseases by the inhalation of gases, the first superintendent being Humphry Davy. His apparatus was constructed by James Watt. In 1794, Beddoes and Watt published their *Considerations on the Medicinal Use of Factitious Airs*.

1795. A second edition of Beddoes and Watt's monograph appears, and contains a letter on the inhalation of ether by Richard Pearson of Birmingham, who also publishes a tract, *A Short Account of the Nature and Properties of Different Kinds of Airs*, in which his ideas are given in greater detail. Pearson states that he has had frequent opportunity of administering ether by inhalation to persons suffering from consumption. He found that it relieved the dyspnoea and promoted expectoration.

1795. The British take Cape Colony from the Dutch.

1797. Jacques Garnerin makes a parachute descent of about 3,300 feet from a balloon.

1798. The battle of the Nile.

1798. Edward Jenner (1749–1823), one of the greatest benefactors of mankind, describes vaccination against smallpox, at that time one of the most dreaded diseases of mankind, in his *Inquiry into the causes and Effects of the Variolae Vaccinae*, which not only saved countless lives, but also opened the door to the study of immunity.

1800. The union of Great Britain and Ireland.

1800. Benjamin Thompson, Count Rumford (1753–1814), founds the Royal Institution of Great Britain, where Humphry Davy soon became a professor, as did Thomas Young (propounder of a theory of colour vision and instrumental in the decipherment of Egyptian hieroglyphics) and Michael Faraday. Although an American, Thompson was knighted by King George IV, made a fellow of the Royal Society and appointed a Count of the Holy Roman Empire.

1800. Fine of Geneva describes a leather endotracheal tube.

1800. Humphry Davy (1778–1829), at this time Superintendent of Beddoes' Medical Pneumatic Institute, issues his *Researches Chemical and Philosophical, chiefly concerning Nitrous Oxide . . . and its Respiration*, which contains the remark, "As nitrous oxide in its extensive operation appears capable of destroying physical pain, it may probably be used with advantage during surgical operations in which no great effusion of blood takes place." Davy deserves great credit for inhaling nitrous oxide in spite of the pronouncement by the celebrated Latham Mitchill that this gas was the dreaded "contagium" or cause of disease. For full details of Davy's life and work, see Cartwright's *English Pioneers of Anaesthesia* (Bristol), John Wright, 1952).
According to Keys (*History of Surgical Anaesthesia*, New York, Schuman (1945), p. 105), William Allen this same year demonstrated in the presence of Astley Cooper and others the results of inhalation of nitrous oxide, noting especially the loss of sensation to pain. This incident is taken from a history of Guy's Hospital written in 1892, and therefore lacks contemporary evidence.

1803. The Battle of Assaye.

1804. Napoleon Bonaparte becomes Emperor of the French.

1805. The Battle of Trafalgar.

1805. Dr. John Warren of Massachusetts uses the inhalation of ether in the treatment of phthisis.

1806. The Holy Roman Empire declared ended.

1806. The Royal Humane Society authorizes special instruments for resuscitation. Somewhat similar to those designed by Kite, they include a silver endotracheal catheter.

1806. Friedrich Sertürner (1743–1841) announces the isolation of morphine (*J. Pharmac. Leipzig*). Not only was this an important event for its own sake, but also it initiated the search for alkaloids and the isolation of the active principle of many substances, which could thereafter be given in definite dosage.

1807. Abolition of the Slave Trade by Britain.

1807. Chaussier designs an endotracheal catheter with a flange of sponge to secure an airtight fit at the glottis.

1807. Von Humboldt and Bonplan describe the manufacture of curare (*Voyage aux Régions Equinoxiales du Nouveau Continent*).

1807. Count Maxime de Puységur publishes his book, *Du Magnétisme Animal*, in which reference is made to "somnambulism" — the hypnotic trance which de Puységur, an ardent admirer of Mesmer, had discovered.

1807. Baron Dominique Jean Larrey (1766–1842) rediscovers the analgesic action of cold, last noticed by Bartholin in 1661, at the Battle of Preuss-Eylau. Inventor of the "Flying ambulance" and a pioneer in the use of intragastric feeding, Larrey was an outstanding surgeon and a faithful servant who was not forgotten in his master's will.

1808. The Peninsular War.

1808. William P. C. Barton, a pupil of Benjamin Rush, publishes his *Dissertation on the Chymical Properties and Exhilarating Effects of Nitrous Oxide Gas.*

1809–1847. Mendelssohn.

1809–1849. Chopin.

1809. William Allen and W. H. Pepys deliver a paper, *On Respiration*, at the Royal Society, wherein they show that the only change which occurs to air on respiration is the substitution of CO_2 for a portion of the oxygen; that, when pure oxygen is breathed, nitrogen is excreted by the lungs; and that the lungs do not completely collapse on expiration, but still contain more than 100 cubic inches of air.

1809. Ephraim McDowell (1771–1830) of Kentucky performs the first successful ovariotomy. The tumour weighed 22½ lb. and the patient survived for a further thirty-three years, dying at 78. Subsequently, McDowell performed seven more ovariotomies.

1811. Sir Benjamin Brodie (1783–1862) delivers a paper on curare at the Royal Society, in which he shows that artificial respiration is capable of supporting life in fully curarized animals. He performed a tracheotomy and inflated the lungs by means of bellows and a cannula. Subsequently, Brodie opposed the introduction of ether anaesthesia: having killed some guinea-pigs by causing them to inhale ether, he pronounced anaesthesia to be dangerous.

1815. The Battle of Waterloo.

1815. The Apothecaries Act lays the basis for medical teaching in England. It was not until 1828, however, that hospital attendance became obligatory for the student.

1815. Nysten (*Dictionary of Medical Science*) speaks of the inhalation of ether as familiarly known for mitigating the pains in colic.

1816. René Laennec (1781–1826) invents the stethoscope. He invented many of the terms now familiar, such as râles, pectoriloquy, aegophony and bronchophony.

1817. It is possible that ether was used as an anaesthetic in Edinburgh at about this time, but, in the absence of contemporary evidence, the incident described in the *Edinburgh Medical and Surgical Journal* of April 1847 is somewhat doubtful. It is said that a bone was removed from the throat of a woman, the operation having proved impossible without the assistance of an inhalation of ether (vide a letter by Dr. Douglas Guthrie in the *Lancet*, 1947, **2**, 921).

1818. James Blundell (d. 1877), on December 22, read to the Medico-Chirurgical Society of London an account of a transfusion of 12–14 ounces of blood. Blundell reported a further six transfusions in 1824, and described his "Impellor"; he subsequently carried out a number of useful experiments on animals proving that life might be saved after blood loss by the infusion of comparatively small quantities of blood.

1818. An article appears in the *Quarterly Journal of Science and Arts* in which it is stated that "when the vapour of ether, mixed with common air, is inhaled, it produces effects very similar to those occasioned by nitrous oxide." A method of vaporization of ether by means of a bottle into the upper part of which a tube could be introduced for a variable distance is also described. The article, which is anonymous, has usually been ascribed to Michael Faraday (1791–1867), but there is no proof that he was in fact the author.

1819. Stockman (U.S.A.) demonstrates the exhilarating effects of nitrous oxide.

1819. John Dalton reads a paper, subsequently published in the *Annals of Philisophy*, entitled "Memoir on Sulphuric Ether". This is the classic paper on the chemistry and physical properties of ether.

1821. Pièrre Bretonneau (1778–1864) reads a paper before the Paris Académie de Médecine in which he asserts that "croup" "malignant angina" and "scorbutic gangrene of the gums" are a specific disease for which he proposes the name "diphtheritis".

1821. Joseph Claude Anthelme Récamier (1774–1856), Professor of Medicine at the Collège de France, performs the first operation under intentional anaesthesia in modern times: the application of the cautery while the patient was under hypnosis. This epoch-making event appears to have passed unnoticed by the historians of anaesthesia.

1823. Thomas Wakley founds the *Lancet*, which, from its first issue, courageously attacked the corrupt management of hospitals and the inadequate requirements for the training of doctors. Wakley became the target of abuse, assault and libel actions, but persisted in his policy until he had caused far reaching reforms to be made.

1824. Henry Hill Hickman (1800–1830) who had already carried out the first planned animal experiments on surgical anaesthesia with carbon dioxide, writes his *Letter on Suspended Animation* to T. A. Knight, later modified and published. In 1828 Hickman addressed a communication to King Charles X of France, requesting that his method of anaesthesia should be considered by the Académy de Médecine. A committee was formed but reported adversely; in the plenary session, Baron Larrey is said to have been the only person to have commented favourably on Hickman's proposals.

1825. François draws attention to morphine-like substance present in lettuce at the time of seed-bearing.

1825. Waller and Doubleday, independently, employ blood transfusion in obstetric haemorrhage. Doubleday's patient who received 14 oz. showed a striking improvement. Waller continued to use transfusion, and reported a successful case in 1859.

1825. Charles Waterton (1782–1865) publishes his *Wanderings in South America*, which contains an extensive and reasonably accurate account of curare.
1827. The Battle of Navarino secures the establishment of the Kingdom of Greece.
1827. Leroy shows that the use of the bellows in artificial respiration may cause pulmonary damage and, in the following year, describes a spatula to aid in endotracheal intubation.
1827. Richard Bright (1789–1858), in his *Reports of Medical Cases*, shows the connexion between diseased kidneys and dropsy.
1827. Boussingault and Roulin prepare a partially purified extract of curare.
1828. The repeal of the Test Act.
1828. Cap (Lyons) describes an endotracheal tube and pump for resuscitation.
1829. William Wright, in his *On the Varieties of Deafness*, shows that, in certain circumstances, carbon dioxide can act as a local anaesthetic.
1829. The French surgeon Cloquet performs a painless mastectomy with the aid of hypnotism.
1830. Opening of the Liverpool and Manchester railway.
1831. Samuel Guthrie (1782–1848) of New York State discovers chloroform ("Guthrie's Sweet Whisky"). He is quickly followed by Eugène Soubeiran in France and Justus von Liebig in Germany; von Liebig also discovers chloral.
1831. O'Shaughnessy of Newcastle upon Tyne shows that during cholera, the fluids and salts in the blood are greatly reduced, with a corresponding increase in fluids and salts in the excreta.
1832. During the cholera epidemic, Thomas Aitchison Latta of Leith, relying on O'Shaughnessy's observation, employs intravenous saline solution with great success in the treatment of severe cholera.
1831. The Reform Bill is passed. The Anatomy (Warburton's) Act institutes the licensing of medical schools and also legislates for the supply of subjects for the teaching of Anatomy, thus freeing the doctors from the activities of the "Body Snatchers",
1832. Wardrop advocates anaesthesia by bleeding to syncope.
1833. Marshall Hall (1790–1857) demonstrates that the spinal cord is a chain of segments whose functional units are separate reflex arcs. His name is associated with a method of artificial respiration, performed by rolling the prone patient to each side, which was an improvement on the earlier method of rolling the patient on a barrel.
1834. J. B. A. Dumas (1800–1884) discovers the chemical composition of, and gives its present name to, chloroform.
1835. Robert James Graves (1797–1853) ("He fed fevers") describes exophthalmic goitre.
1836. Lafargue injects a paste containing morphine under the skin with a blunt syringe, first making small incisions in order to insert the nozzle.
1837. Liégard revives the method of local analgesia by compression of the limb.
1839. Taylor and Washington in U.S.A. repeat Lafargue's method of injecting morphine (vide 1836).
1839. The following is quoted from Clutterbuck's *Lectures on Bloodletting* (vide Clement, *Anesthesiology* (1953), **14**, 480): "In one of the great hospitals of the metropolis a case occurred lately where 128 ounces of blood were drawn at one time in order, by inducing syncope, to facilitate the reduction of a dislocation of the thigh. The patient lived a week afterwards, and then, as is said, died from inflammation of the vein punctured."
1839. Edwin Chadwick (1800–1890) succeeds in having a Sanitary Commission created.
1839. John Scoffern, in *Chemistry no Mystery, or a Lecturer's Bequest*, gives an account of nitrous oxide and its intoxicating effects. This is one of the few scientific books illustrated by Cruikshank ("Phiz") and contains a well-known frontispiece entitled "Laughing Gas".
1840. Penny Postage introduced under Rowland Hill's scheme.
1840. The "Health of Towns Association" founded by Southwood Smith (1788–1861).
1841. Death of Sir Astley Cooper (b. 1768).
1841. Robert Schomburgk, *On the Urari*, describes the plants used in making curare.
1842. Robert H. Collyer, an imigrant to the U.S.A. from Jersey, extracts a tooth painlessly from Mrs. Allen of Philadelphia with anaesthesia achieved with alcohol. He had previously reduced a dislocated hip in an intoxicated negro without causing pain.
1842. R. M. Glover of Newcastle upon Tyne describes (in his Harveian Prize Essay) the effect of chloroform and other halogenated substances when injected into the bloodstream of animals. He observed, among other effects, depression of the blood pressure and respiration.
1842. In January, William E. Clarke, who had frequently participated in "Ether Frolics", in Rochester, Minn., administered ether from a towel to a Miss Hobbie while one of her teeth was extracted by Elijah Pope. Neither Clarke nor Pope published an account.
1842. In March, Crawford Williamson Long (1815–1893) of Jefferson, Georgia, administered ether to a man called James Venable and excised a sebaceous cyst. Long carried out several operations under ether, but finally gave up its use. He published no account of his cases until after the demonstration of ether anaesthesia by Morton.
1842. In October, W. Squire Ward of Wellow, near Ollerton, Notts, painlessly amputated a leg of James Wombwell who had been hypnotized by W. Topham of the Middle Temple.
1843. James Braid (1795–1860) publishes his *Neurypnology*, in which he showed that the "mesmeric influence" was entirely subjective, and that no fluid or other substance passes from the operator to the patient.
1843. John Elliotson (1791–1868) issues his *Numerous Cases of Surgical Operations without Pain in the Mesmeric State*, in which he uses the word "anaesthesia", a word which he was to use

again in the modern sense in his Harveian Oration of July 1846.

1843. Oliver Wendell Holmes (1809–1894), poet and man of letters, issues his essay *On the Contagiousness of Puerperal Fever*, in which he showed that the contagion of erysipelas and puerperal fever was the same and that the disease was frequently carried from one patient to another by the physicians.

1844. F. Rynd of Dublin uses an ingenious trocar for injecting morphine subcutaneously in the treatment of tic douloureux. He did not publish an account until 1861.

1844. E. E. Marcy of Hartford, Conn., "administered the vapour of rectified ether in my office to a young man . . . and after he had been rendered insensible to pain, cut from his hand an encysted tumour the size of an English walnut."

1844. December 10: Horace Wells of Hartford, Conn., attends a demonstration on Laughing Gas by Gardner Quincy Colton. Impressed by what he sees, the following day he allows Colton to administer the gas to him, while another dentist, Riggs, extracts one of Wells' teeth. Wells used nitrous oxide in some dozen cases with success and then, later in December, obtained permission to demonstrate his method of anaesthesia at the Massachusetts General Hospital. The demonstration was a failure and Wells abandoned the use of nitrous oxide.

1844. Dr. E. R. Smilie of Boston, claimed (in 1846) that he had rendered a certain John Johnson insensible to pain for the opening of an abscess in the neck by the use of an ethereal tincture of opium.

1845. Erichsen advocates the use of oxygen in the resuscitation of drowned persons. Depaul modifies Chaussier's endotracheal tube (vide ante, 1807), giving it a terminal, instead of a lateral, eye.

1845. George Wilson, Lecturer in Chemistry at Edinburgh, advocates the use of oxygen in resuscitation, describes its method of preparation and gives directions for constructing a sort of oxygen tent and its method of use. He also advocates the use of oxygen in diving bells and suggests the absorption of carbon dioxide by sulphate of soda and lime.

1846. Repeal of the Corn Laws.

1846. James Esdaile (1808–1859) publishes his *Mesmerism in India and its Practical Application in Surgery and Medicine*. He had performed his first major operation under hypnotism in 1845; he reported in all 261 cases, with a mortality of 5.5 per cent, and a committee reported very favourably on his results.

1846. March: Ducos recounts experiments on animals with ether, in which insensibility with recovery was noted. Like Glover (vide ante, 1842), Ducos failed to grasp the implications.

1846. September 30: William Thomas Green Morton (1819–1868) administers ether to Eben Frost for the extraction of a tooth. October 16: Morton anaesthetizes Gilbert Abbott at the Massachusetts General Hospital, the surgeon being Dr. John C. Warren (1778–1856). The patient suffered from a vascular tumour on the left side of the neck, which was to have a ligature passed around it in order to reduce its blood supply. The ether was placed in a glass vessel, containing a sponge, with two orifices, one of which had a mouthpiece attached to it. The patient was asleep within 4 minutes, and the inhaler was then removed, the anaesthetic not being administered during the operation. An incision about 3 inches in length was made over the tumour, a curved needle was then passed round it, and the ligature fastened. During most of the time, the patient showed no sign of sensibility, but a short time before the end of the operation he moved his head, body and limbs, and began to mutter. On recovering consciousness, he declared that he had felt no pain, but simply a scraping sensation. Dr. Warren, expressed his satisfaction in the words: "Gentlemen, this is no humbug"; and Dr. Henry J. Bigelow, who was one of the numerous spectators, with greater realization of the dignity of the occasion, announced, "I have seen something today which will go round the world."

(To be continued)

Brit. J. Anaesth. (1957), **29**, 584

HYPOXIA IN MAN

Induced Unconsciousness, with Reflex and Muscle Control, The Logical Approach to the Three Dimensional Study of Cellular, Cardiorespiratory and Cerebrospinal Hypoxia

BY

PALUEL J. FLAGG

President of the National Resuscitation Society, Inc.

GENERAL ANAESTHESIA IN THE HUMAN BEING, AN ESSENTIAL DISCIPLINE FOR ALL PHYSICIANS

The multiplication of anaesthetic agents and techniques with the drift from a control by gases to a control by drugs, during the last three decades has had a double effect.

(1) It has segregated interest in anaesthesia to a restricted professional-technical group.

(2) It has sharply reduced the overall interest in anaesthesia among resident house officers who no longer are required to give anaesthetics, and who have no intention of becoming anaesthetists.

It is believed that this elimination of the house officer from a tour of duty in anaesthesia has been most unfortunate. Exclusion from this fundamental clinical routine has been predicated and apparently justified by a desire for an improved and safer field for surgery, aided and abetted by students and house officers who are not interested in serving as technicians or in becoming anaesthetists.

As the end in view was limited to anaesthesia and the technique looked upon as merely a convenience for the surgical service, the change has come easily.

However, the student, the resident and presently the general practitioner has suffered an irreparable loss. He is no longer familiar with the unconscious patient, and with the management of the abnormal physiology which accompanies or may precipitate unconsciousness. He is no longer sensitive to *man—alive*, the three dimensional view of form, function and time. Sensitiveness comes only when one is required to control this integration in unconscious man, the man in whom induced control has taken the place of voluntary or automatic control. If one is not responsible for, and obliged to direct the factor of timing, this third dimension is likely to be overlooked altogether.

Time operates by determining the instant, the degree and the duration of function. Its recognition allows the instantaneous freezing of the fluidity of function. It permits a precise diagnosis, or the application of a desirable act, as it were in functional transit. The effect of a gas or drug either progresses or retrogresses. It is never static. Timing determines the correct instant of effect or action. Form and function may be taught, time must be experienced.

The factor of timing becomes apparent for example, in the variable hazard of retro-orbital block for intra-occular surgery. Suppose morphine has been given and respiratory obstruction develops. The aspiration effect of the large vessels is reduced and blood dams back into the right ventricle. The veins of the systemic circulation, including those of the head and neck, become engorged; at this instant the swollen orbital veins present an enlarged area for trauma during injection for retro-orbital block.

ACCIDENT AND DISEASE

To become familiar with the phenomena of unconsciousness induced and controlled by anaesthesists, is to be at home with the phenomena of unconsciousness induced by accident and disease, i.e., drowning, foreign body obstruction, electrocution, carbon monoxide poisoning, cerebral haemorrhage, terminal poliomyelitis and drug poisoning. The sequence of depression,

rigidity and relaxation in anaesthesia is paralleled by the depression, spasticity and flaccidity of hypoxia. The physics of gas therapy and the mechanics of relief are identical.

The chief value of general anaesthesia for *all* physicians is, therefore, to provide a means of becoming acquainted with the abnormal physiology of the unconscious patient.

Given this incentive and objective the student may well become eager for opportunities to administer general anaesthetics. The anaesthetist will become intrigued by the broader view of unconsciousness from its many causes, and he will develop more respect for the integrity of normal physiology. He will become more conservative in subordinating these normal processes to depressive and lethal drugs. It will become clear that while increased demands upon normal function may fall within physiological limits, suppression of function may set off a chain reaction resulting in morbidity and mortality.

INTERDEPARTMENTAL CORRELATION

Interdepartmental correlation helps to break down barriers in the field of medical education. This does not mean, however, that specialists in one field or department should do independent research in another, i.e., the anaesthetist is not expected to carry on fundamental research in physiology independent of the authority, direction, and control of this department. Instead of assuming the role of pathfinder, the anaesthetist may well spend more time in the department of physiology as an advanced student. Interdepartmental correlation suggests that basic knowledge should be common knowledge. The physiologist and the pharmacologist should visit the operating room as frequently as the pathologist, preferably after a short course in operating room routine.

Familiarity with this three dimensional aspect of form function and timing will not only clarify the view when interference occurs through accident, or disease, but the indications presented by this superimposed pathology will be seen to carry with them clear indications for treament.

The following suggestions are offered for the interdepartmental correlation of the problem of hypoxia, from its metabolic, cardiorespiratory and cerebrospinal point of view. A strong emphasis is placed on clinical opportunities to activate this academic information. The magnificent integration of the marvellous complexity of *man—alive,* should intrigue rather than discourage interest. After all so much time and effort has been devoted to becoming acquainted with the various systems and functions of the organism, that reasonable attention can certainly be devoted to a study of the total living man.

ACADEMIC INSTRUCTION

Undergraduate Interdepartmental Correlation.

Anatomy. The structures of the upper airway by postmortem sections and general orientation by peroral endoscopy are to be featured. Relations and measurements in adult and infant should be stressed. Emphasis would be placed upon the anatomical location of accessible blood vessels in the extremities, for purposes of transfusion, medication, intravenous anaesthesia and analgesia.

Physiology. A study of infant, child and adult physiology with special reference to muscle tone, reflexes and impaired function as these relate to anaesthesia, resuscitation and inhalation therapy, would be stressed as well as the relative resistance of infant and adult to medication and to progressive hypoxia.

Biochemistry. Demonstrations would be made covering the chemistry of tissues; metabolism; hormones; respiration; water-balance acid-base and functional tests, as these apply to hypoxia. The phenomena of histotoxic hypoxia and the biochemistry of methylene blue, cyanides and alcohol would be examined.

Chemistry and physics. A study would be made of the chemical make-up of anaesthetic and other therapeutic gases with special reference to their diffusion and elimination, as well as the physical behaviour of gases in relation to partial pressures, diffusion and explosive factors, as these may result in hypoxic manifestations.

Pharmacology. Laboratory work dealing with gases and drugs employed to control pain, to save life and to treat clinical disease would be considered. Therapeutic indices, allergy, irreversibility of drugs, detoxification as related to hypoxia would be discussed.

Pathology. Lesions resulting from hypoxia in the cardiorespiratory and cerebrospinal systems

merit special consideration. Reference would be made to blood diseases that influence the action of anaesthetic drugs and gases, such as the anaemias, purpuras and leukaemias.

The pathological effects of the following should be taught:

(1) Poison gases in civilian and battle hazards, toxic gases in industry (carbon monoxide, ammonia, carbon dioxide, hydrogen sulphide, hydrocyanic acid). Histotoxic hypoxia of alcohol and the sulphonamide drugs.

(2) The action of drugs, i.e., hypnotics, narcotics, sedatives, analgesics, anaesthetics, as these appear in postmortem lesions.

(3) Submersion.

(4) Tissue lesions from electrocution.

Special reference could be made to the pathological lesions resulting from asphyxia of the newborn, suffocation and strangulation, as well as from tumours and foreign bodies in the airway. The pathology of terminal poliomyelitis can be discussed from the point of view of hypoxia. The microscopic anatomy of the respiratory tract may be studied with reference to gas exchange, inflammation, and regeneration following trauma, noting particularly granuloma of the vocal chords and tracheal mucosa trauma from endotracheal balloon pressures. The requirements of thoracic surgery in relation to gas pressure control, oxygenation, mediastinal shift, and the treatment of extensive tuberculosis and its complications, must be considered. Special attention would be given to traumatic or surgical collapse and shock, abdominal distention, hypoxic headache following encephalography, pulmonary oedema, pulmonary embolism, atelectasis, massive collapse of the lung, coronary embolus and to infections due to anaerobic organisms such as those of gas-gangrene and tetanus.

Medical jurisprudence. Death from hypoxia should be considered along with the coroners' reports and the rulings relative to operating room deaths. National death returns as these refer to hypoxic accidents may be reviewed, and a survey made of hypoxic deaths occurring under the supervision of the university.

Medicine. Physical examination with reference to post-hypoxic accidents would be stressed. The treatment of disease of a cardiorespiratory, cerebrospinal and metabolic nature could be considered. The physical signs of death as these are determined by the absence of a heart-beat (cardiac arrest), by intracardiac needle, by alteration of the colour of the mucous membranes in the presence of oxygen administration and by retinal haemorrhages would be discussed.

Radiology. The interpretation of radiographs would be taught with reference to the pathology of the airway and the lung, mediastinal shift, malposition and tumours of the trachea, as well as acute infections of the airway.

CLINICAL INSTRUCTION

Interdepartmental Correlation for Resident House Officer and Practitioner. Instruction would feature opportunities to become familiar with the induction, maintenance and recovery from a simple nitrous oxide-oxygen ether anaesthesia; it would include dissertations on the prevention, recognition and treatment of postanaesthetic complications. The technical care of patients with certain diseases by oxygen or helium therapy employed by mask, catheter or tent should be detailed as well as the administrative supervision of technical assistants.

Obstetrics. Asphyxia neonatorum, its incidence, special histology and gross pathology should become familiar to the student. He would be taught to recognize the stages of progressive hypoxia, depression spasticity and flaccidity and their underlying pathology. The indications which this pathology presents for specific treatment would be clarified. Suitable equipment to meet these indications needs to be improvised. Post-treatment pathology would be carefully noted, i.e., reactions following laryngoscopy and intubation for terminal hypoxia.

Paediatrics. The incidence and form of hypoxia in the newborn, the infant and the child would be studied together with adequate emergency treatment.

Surgery. The hypoxia incidental to anaesthesia and surgery would be reviewed and demonstrated by the department of anaesthesia. Acquaintance with the three dimensional man would here be accomplished. Metabolic, cardiorespiratory and cerebrospinal hypoxia as it may be controlled by safe general anaesthesia would be featured. Every

case of general anaesthesia is material for a study of normal physiology. The reaction of normal physiology to pharmacological, physical, pathological and surgical factors incidental to operation would be demonstrated. The expert knowledge of the anaesthetist would be brought to bear to demonstrate without hazard to the patient, familiar and exceptional physiological reactions. The student will be expected to become acquainted with how to maintain the airway of the unconscious patient and adept in simple laryngoscopy in the unconscious relaxed patient; this is the open door to the knowledge of how to treat all types of emergency hypoxia.

Extramural activities. Hypoxia is by no means limited to operating room or ward emergencies. A modern resuscitation service must be provided not only within the hospital for the treatment of asphyxia neonatorum, drugs, narcotics, acute alcoholism, pulmonary complications, anaesthetic overdosage, pathological abnormalities, mechanical obstruction from foreign bodies in the airway and trachea, allergy, terminal poliomyelitis, polyneuritis, and facial diplegia; but in every ambulance servicing hypoxia accidents which occur in public places, for example, gases used industrially, i.e., carbon monoxide, refrigerants, chemical fumes, fumigation, submersion, firefighting, electrocution, strangulation, hanging, suffocation from soft materials and from external pressure of moving objects (e.g. automobiles, elevators, laundry machines), from collapse of buildings, from earthmounds, sand, coal, landslides in manholes and declivities. The student will understand that his work has a bearing on public health scarcely second to his hospital activity.

Military. Opportunities could be offered for contact with the medical departments of the army and navy as these departments reflect specialized hypoxic hazards.

Reference would be made to the effects of high altitude acceleration and deceleration hypoxia, as these are met in air forces. Submarine air conditioning, and escape techniques would be explained. Compression and decompression through the use of airlocks in the army and in industry would be described.

The student must be advised of his responsibility to instruct fire, police, industrial first aid and lay organizations in the emergency care of hypoxia.

CONCLUSIONS

While hypoxia cuts across the entire field of medicine, appearing both as a symptom and a cause of death, its urgency demands that it be immediately identified, segregated and treated as a potential fatality if the present national mortality rate of at least 50,000 a year is to be reduced.

The current practice of pointing out the danger of hypoxia in its many fields at irregular or at long intervals over the years of medical instruction, has failed to bring to a focus the tragic significance of the problem.

An early strong and sustained effort to effect permanent interdepartmental correlation respecting hypoxia is imperative. Because of the loss of lives involved in delay, the desire for unique institutional experimental approaches to the need may perhaps be sacrificed in favour of an immediate two-fold programme.

(1) Academic interdepartmental correlation as suggested or in some modified form for undergraduates.

(2) Clinical correlation calculated to activate this material for graduates.

(*a*) By sponsorship through a permanent committee representing surgery, obstetrics, paediatrics, internal medicine, anaesthesia, pathology, and military medicine.

(*b*) By familiarity with induced and controlled unconsciousness through the teaching of anaesthetists. A knowledge of the unconscious patient is the logical approach to the treatment of metabolic, cardiorespiratory and cerebrospinal hypoxia.

Printed in Great Britain by
JOHN SHERRATT & SON
Park Road, Altrincham

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VOLUME XXIX No. 12 *Published monthly* DECEMBER 1957

Annual subscription (post free): Inland £3 15*s.*: *Overseas* £4 4*s.*: *U.S. and South Americas* $12.00

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JOHN SHERRATT & SON *Publishers* PARK ROAD ALTRINCHAM ENGLAND

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